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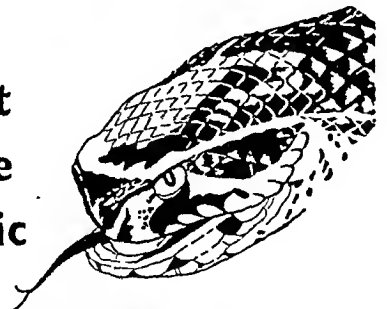
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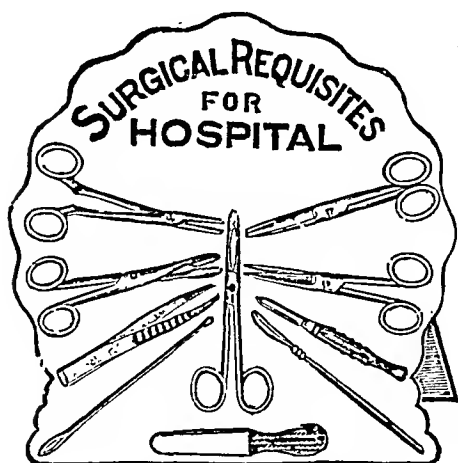
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## Original Articles

### CHEMOTHERAPEUTIC STUDIES IN THE TREATMENT OF MENINGOCOCCAL AND PNEUMOCOCCAL MENINGITIS

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A SUPPLY of diaminodiphenyl-sulphone glucoside was placed at our disposal by Dr. G. A. H. Buttle of the Wellcome Research Laboratory for trial in meningitis.

A large number of cases are admitted every year to the Campbell Hospital, and, with the permission of its superintendent, Col. Mallya, I.M.S., the value of this drug in the treatment of meningitis was tested in a series of cases. Such cases are admitted throughout the year in Calcutta, but the disease assumes epidemic proportions during the cold weather months of December, January and February. Our experiment commenced in the middle of November 1938 and ended at the end of February 1939 when the supply of the drug under trial was temporarily exhausted; a few additional cases were treated at the end of March when a further supply was received.

The cases were not selected, but, on admission, alternate cases were treated with anti-meningococcal serum (which series served as a control) and with the sulphone compound. All cases were admitted to the same ward and were under the immediate care of one of us (B. C. C.) who is in joint medical charge of the infectious diseases wards at the Campbell Hospital.

Cases in the drug-tested series were given orally 0.5 gramme of the sulphone glucoside compound every two hours up to a maximum of 3.0 grammes daily. Its administration was continued until the cerebro-spinal fluid became clear or when methæmoglobinæmia appeared to be imminent. Spectroscopic examination of the blood for the appearance of methæmoglobin and sulphæmoglobin bands was carried out, and the amount of drug administered was reduced or stopped altogether when the appearance of any one of these bands was noted. All sulphates and sulphur-containing compounds were withheld and the administration of purgatives was avoided as far as possible. The drug, which is in tablet form (0.25 gm. per tablet), was always administered orally, the tablets being crushed and given as a suspension in water.

The control series received polyvalent anti-meningococcal serum both intrathecally (I T) and intravenously (I V).

Usually about 40 c.cm. of serum (20 c.cm. intrathecally and 20 c.cm. intravenously) was administered every morning as long as symptoms persisted. Seriously ill patients were given a similar amount again in the evening. Occasionally 40 c.cm. was administered intravenously in addition to a variable amount given intrathecally.

In both series the patients were given in addition potassium bromide grs. x, when it was considered necessary, and a mixture containing liquor hydrargyri perchloridi, half a drachm, and potassium iodidi, five grains, three times daily, until convalescence was established. Lumbar or cisternal puncture was performed frequently as long as symptoms persisted. The cerebro-spinal fluid in all cases was examined bacteriologically, to establish diagnosis. The fluid was examined microscopically by the preparation of films (after centrifuging when necessary) and staining by Gram's method. It was also seeded on to pigeon-blood agar for the isolation of meningococci.

Thirty-three cases were treated according to the procedure above outlined; 24 of these were meningococcal infections, seven were pneumococcal, and two were bacteriologically negative. The detailed results obtained are given in the tables.

Gram-negative diplococci resembling meningococci were seen to be present, by microscopic examination, in the cerebro-spinal fluid of all the patients included in table Ia.

From a study of table Ia, it will be observed that of the five patients that died one (case 25) received only one gramme of the drug. This case was actually a control that was put on diaminodiphenyl-sulphone glucoside when the condition appeared to be hopeless and death inevitable. Another (case 18) received 5 grammes and died after only 36 hours' stay in hospital. Apart from these two, the minimum amount of drug administered to the patients that died was 13.5 grammes (case 16) and the maximum 30 grammes (case 13). The latter was doing exceptionally well, convalescence seemed to have been established and the administration of the drug had been stopped for six days when the patient relapsed. His temperature rose steeply, the cerebro-spinal fluid which had been clear became turbid again and was under pressure; headache, stiffness of the neck, etc., soon became progressively worse until death supervened. The administration of the drug was recommenced but it appeared to have no effect. The minimum amount of drug administered in the recovered cases was 10.5 grammes and the maximum was 30 grammes, so that three at least of the fatal cases received an amount of drug equal to that received by those that recovered.

TABLE Ia (DRUG-TREATED GROUP)  
Details of cases treated with diaminodiphenyl-sulphone glucoside alone

Case number	Amount of drug given (in gms.)	Result	Days in hospital	Bacteriological examination	REMARKS
1	10.5	Cured	8	N. G.	Absconded; seen one month later in good health. Relapsed and died.
3	14.0	"	6	I	
5	35.0	"	22	C.	
13	30.0	Died	21	I	
16	13.5	"	6	II	
18	5.0	"	1½	N. G.	
23	28.0	Cured	20	C.	
24	30.0	"	24	I	
25	1.0	Died	2½	N. G.	
27	30.0	Cured	58	I	
30	20.0	Died	10	II	
36	17.5	Cured	14	C.	

I = Group I meningococci isolated.  
II = Group II meningococci isolated.  
C. = Contaminated.  
N. G. = No growth.

TABLE Ib (CONTROL GROUP)

Details of cases treated with polyvalent anti-meningococcal serum that served as controls for the cases shown in table Ia

Case number	AMOUNT OF ANTI-MENINGOCOCCAL SERUM GIVEN (IN C.C.M.)		Result	Days in hospital	Bacteriological examination
	I T	I V			
2	40	60	Died	4	N. G.
4	60	190	Cured	22	I
8	60	60	Died	1½	II
10	20	20	"	1½	N. G.
11	65	230	"	10	N. G.
15	47	100	"	4	C.
17	120	390	"	18	C.
19	40	270	Cured	18	N. G.
21	30	240	"	23	C.
26	90	120	Died	3	I
28	10	40	"	22 (hours)	C.
29	60	330	Cured	20	N. G.
33	110	170	"	9	N. G.
38	50	140	Died	4	N. G.

Gram-negative diplococci resembling meningococci were seen to be present, by microscopic examination, in the cerebro-spinal fluid of all, excepting two patients included in the above table. The two exceptions were cases 19 and 33.

There were therefore 12 proven meningococcal infections of which nine were fatal. Examining the cases that died there were three that remained less than 48 hours in hospital. Excluding these three the minimum amount of anti-meningococcal serum administered was 100 c.cm. (40 I T and 60 I V) during four days while the maximum was 520 c.cm. (120 I T and 390 I V). To those that recovered, 250 c.cm.

was the least amount given and the maximum 390 c.cm.

TABLE Ic (PNEUMOCOCCAL MENINGITIS GROUP)  
Details of the pneumococcal meningitis infections treated with diaminodiphenyl-sulphone glucoside

Case number	Amount of sulphone compound given (in gms.)	Result	Days in hospital	REMARKS
6	28	Death	19	Improved then relapsed and died.
7	3	"	1½	
12	2	"	1	
20	6	"	2	Improved then relapsed and died.
22	47	"	49	
31	1½	"	1½	
34	3	"	1½	

The pneumococcal infections were diagnosed microscopically; the presence of large numbers of Gram-positive lanceolate diplococci, generally capsulated, made identification easy. The pneumococci were isolated in all cases after primary inoculation into mice. Type pneumococcal sera were not available so that it was not possible to determine the serological type of the pneumococci isolated. Anti-pneumococcal serum for treatment purposes was much too expensive and could not be provided by either the patient or the hospital authorities. All the seven patients died so that diaminodiphenyl-sulphone glucoside appears to be of no value in pneumococcal infections. In two cases death was delayed to 19 and 49 days after admission. These cases improved; consciousness was regained, fever had subsided, the cerebro-spinal fluid though not completely clear was hazy, pneumococci were absent and the general condition was very much improved; both cases relapsed and pneumococci again reappeared in the cerebro-spinal fluid in enormous numbers

and death followed, one 19 days and the other 49 days after admission.

A short summary of the results obtained during the course of this trial is given below.

TABLE II

*Summary of results obtained in the preliminary trial*

	DRUG-TREATED SERIES				SERUM-TREATED SERIES			
	Number	Cured	Fatal	Percentage mortality	Number	Cured	Fatal	Percentage mortality
Meningococcal meningitis.	12	7	5	41.7	12	3	9	75
Pneumococcal meningitis.	7	..	7	100	..	..	..	..
Bacteriologically negative cases.	..	..	..	..	2	2	..	..

From table II it will be observed that there were 41.7 per cent deaths in the drug-treated series as compared with 75 per cent in the control series for the cases that were found by microscopic examination to be meningococcal infections. The percentage of deaths in the Campbell Hospital during the past three years for meningitis was between 60 to 70 per cent, so that these results suggest that the administration of diaminodiphenyl-sulphone glucoside had a beneficial effect in the treatment of meningococcal meningitis.

The experiment was next modified so that the drug-treated cases also received anti-meningococcal serum. The action of sulphonamide compounds is not exactly determined. It appears, by exerting a bacteriostatic action, to keep the number of the invading organisms within manageable limits, enabling phagocytosis by the leucocytes. Branham and Rosenthal (1937), in an experimental study of sulphanilamide in meningococcus and pneumococcus infections in mice, came to the conclusion that serum combined with drug therapy gave much better results than either alone. They suggested a synergic action since increased effectiveness of the combined therapy was greater than the added effect of drug and serum alone. Fleming (1939), at a meeting of the section of Obstetrics and Gynaecology of the Royal Society of Medicine, said that the new chemotherapeutic agents had been shown to have rather a bacteriostatic than a bacteriocidal action. The chief result of the drugs was interference with growth of organisms and the actual destruction of the invaders was completed by the natural defensive mechanism of the body. The defensive mechanism could be increased passively by serum therapy or actively by vaccine therapy.

In the succeeding experiment 45 cases were treated, twenty-four received anti-meningococcal

serum as well as diaminodiphenyl-sulphone glucoside orally and a second series of 21 cases anti-meningococcal serum. The details of the results obtained are given in the following tables:—

TABLE IIIa

*Details of cases treated with diaminodiphenyl-sulphone glucoside and anti-meningococcal serum*

Case number	Amount of drug given (in gm.)	AMOUNT OF ANTI-MENINGOCOCCAL SERUM GIVEN (IN C.C.M.)		Result	Days in hospital	Bacteriological examination
		I T	I V			
35	24	40	160	Died	25	I
40	2	40	50	"	37	Nagg
41	38	150	390	Cured	18	Nagg
42	33	130	140	"	23	Nagg
43	18	180	180	"	8	N. G.
44	18	110	160	"	50	Nagg
45	22	170	300	"	4	I
48	7.5	90	90	Died	1	N. G.
49	2.5	10	70	"	17	N. G.
50	22	140	310	Cured	20	II
51	19	150	240	"	10	I
52	15	30	170	"	14	N. G.
53	30	150	230	Died	21	N. G.
54	24	115	180	Cured	21	II
55	5	40	40	Died	16	I
57	18	122	255	Cured	14	Nagg
58	17	100	200	"	26	N. G.
60	24	150	310	"	15	N. G.
61	14	80	210	"	15	II
67	14	110	180	"	13	N. G.
93	27	130	160	"	14	Nagg
94	13	110	180	"	12	I
100	14	40	120	"	2	Nagg
102	6	40	30	Died		

Nagg = Meningococci isolated not agglutinable by group meningococcal sera.

Gram-negative diplococci resembling meningococci were observed, by microscopical examination, to be present in the cerebro-spinal fluid of all but two patients included in table IIIa. The two exceptions were cases 44 and 49.

From table IIIa, it is observed that of the 22 meningococcal meningitis cases six were fatal, giving a mortality rate of 27.3 per cent. Of the six that died one (case 40) received only 2.5 grammes and died within 12 hours of admission. Three others (cases 48, 55 and 102) received 7.5, 5.0 and 6.0 grammes respectively, so that very inadequate amounts of the drug had been administered to four of the six patients that died.

It is felt that diaminodiphenyl-sulphone glucoside should be administered to dangerously ill patients such as these by other routes in addition to the oral one in an endeavour to obtain quicker action. In a private communication we were informed by Dr. Buttle that the drug acts best when administered orally, and,



as we lacked personal experience, we thought it advisable to continue the administration of the drug by the oral route only.

Now, however, it is felt that in desperately-ill patients the drug should be administered by other routes in addition to the oral, in an endeavour to obtain quicker action. Failure in this direction will prove a great drawback in the value of this compound in the treatment of meningitis, at least in Calcutta where most of the patients are brought for treatment when the disease is well advanced and the patient unconscious and dangerously ill. Regarding the two remaining fatalities in this group, one (case 35) appeared to be progressing favourably, the administration of the drug and serum was stopped on 19th January (13 days after admission), but the patient relapsed on the 25th and died on the 30th. He had been receiving 2 grammes diaminodiphenyl-sulphone glucoside from the 6th to the 17th January, the dose was reduced to 1 gramme on the 18th and stopped on the 19th. The readministration of serum and drug after relapse appeared to have no effect. The other (case 53) had been given 3 grammes of the drug daily from the 23rd to the 29th, the patient's condition had improved greatly, his temperature had dropped to 98°F., the cerebro-spinal fluid was almost clear and the tension reduced, though meningococci were still present in the fluid. On the 30th, the amount of drug administered was reduced to 2 grammes daily until 2nd February. During those four days, though meningococci were constantly present in the cerebro-spinal fluid, the patient's general condition was steadily improving. The drug was further reduced on the 3rd to 1 gramme daily, when the patient's temperature rose to 102°F., the cerebro-spinal fluid became turbid and teeming with meningococci, the general condition rapidly deteriorated and the patient died next morning. Anti-meningococcal serum had been given almost daily either intrathecally, intravenously or both, from the day of admission to the day of death. It appears to us that the administration of the drug in the larger doses should have been continued as long as meningococci were present in the cerebro-spinal fluid. The patient had developed no untoward symptoms of toxicity and the drug could have been continued in the larger doses until either meningococci could not be found in the cerebro-spinal fluid, or toxic symptoms due to drug administration supervened.

As regards the patients that recovered, the course of the disease appeared to progress slowly towards recovery. There were no dramatic results; seriously ill patients remained so for 24 days, then slowly improved until convalescence was established. Meningococci generally could not be found by microscopic examination in the cerebro-spinal fluid collected 36 to 48 hours after the administration of the drug, though they were found to be numerous previously.

In most of the drug-treated cases a slight rise of temperature was noticed a few days after the patients had apparently recovered and convalescence was established. Lumbar puncture was performed in a few such cases and the cerebro-spinal fluid was found to be clear and under normal pressure. There was no headache, no stiffness of the neck muscles, etc., and the patients' general condition continued to improve. In short, the patients appeared to be well, except for the slight fever. The temperature soon returned to normal when the administration of the drug was discontinued.

TABLE IIIb (CONTROL GROUP)

*Details of cases treated with polyvalent anti-meningococcal serum and serving as controls for the serum-plus-drug group shown in table IIIa*

Case number	AMOUNT OF SERUM GIVEN (IN C.C.M.)		Result	Days in hospital	Bacteriological examination
	I T	I V			
39	20	60	Died	19/24	C.
46	80	110	"	6	II
47	70	140	"	10	C.
56	100	140	Cured	9	I
62	70	140	"	10	Nagg
63	70	140	Died	7	II
64	70	200	Cured	15	I
65	30	130	Died	6	I
66	40	120	"	3	C.
69	60	140	Cured	8	N.G.
70	135	259	"	38	I
72	70	140	"	12	N.G.
73	60	80	Died	4	C.
74	90	160	Cured	16	N.D.
74A	100	160	Died	8	N.G.
79A	60	50	"	3	II
59	125	260	"	16	I
88A	50	60	"	4	II
96	60	120	Cured	13	N.D.
97	100	100	Died	6	C.
98	90	180	Cured	18	N.G.

N.D. = Not done.

Gram-negative diplococci resembling meningococci were seen to be present by microscopic examination in the cerebro-spinal fluid of all the patients included in the above series except one (case 69).

In table IIIb there are 20 meningococcal infections. Of these 12, or 60 per cent, died, all of whom, excepting one, were treated in hospital for three or more days. The minimum amount of anti-meningococcal serum administered to these cases was 110 c.c.m. and the maximum 385 c.c.m., while 180 c.c.m. was the minimum and 385 c.c.m. the maximum amount of serum administered to the cases that recovered. The administration of anti-meningococcal serum was on the whole unsatisfactory, in that a sufficient amount of it was not always available. The serum used was that prepared by a local firm. Parke Davis serum was given to a few cases when it was

available; later the stock was completely exhausted.

The result of this second and modified trial is summarized in table IV.

TABLE IV

*A summary of the results obtained in the second and modified trial*

	DRUG AND SERUM TREATED SERIES				SERUM TREATED (CONTROL) SERIES			
	Number	Cured	Fatal	Percentage mortality	Number	Cured	Fatal	Percentage mortality
Meningococcal meningitis.	22	16	6	27.3	20	8	12	60
Bacteriologically negative cases.	2	1	1	..	1	1	..	..

Here again the percentage mortality among 22 cases of meningitis treated with diamino-diphenyl-sulphone glucoside is very much lower than that obtaining in the control series, the respective rates being 27.3 per cent for the drug-treated series and 60 per cent for the control series. It was unfortunate that the trial could not be continued longer. The figures in each group are much too small to warrant one drawing a definite conclusion. But taking the two series as a whole it can be stated that a statistically significant reduction in the mortality rate is obtained when meningococcal meningitis is treated with the sulphone compound as compared with a similar series of cases not so treated.

The following table summarizes the result obtained in the combined series:—

TABLE V

*A summary of the combined results obtained in both the first and second trials*

	DRUG TREATED				CONTROL SERIES			
	Number	Cured	Fatal	Mortality rate per cent	Number	Cured	Fatal	Mortality rate per cent
Meningococcal meningitis.	34	23	11	32.35	32	11	21	65.6
Pneumococcal meningitis.	7	..	7	100	..	..	..	..
Bacteriologically negative cases.	2	1	1	..	3	3	..	..

*Toxicity.*—Buttle *et al.* (1937) report that 0.3 gramme of 4:4 diaminodiphenyl sulphone when administered in a single dose to a healthy individual caused no symptoms, but blood collected from the individual five hours later

contained methæmoglobin. In a personal communication to one of us Buttle states that 3 grammes given daily for a week, with resting periods of one to two weeks, to cases of sub-acute endocarditis, caused considerable cyanosis and hyper-excitability. In mice, a single dose of 20 mgm. or daily doses of 10 mgm. by mouth are well tolerated by animals weighing 20 grammes but produced symptoms of hyper-excitability in four to five days.

In this experiment, spectroscopic examination of the blood of the patient's receiving diamino-diphenyl-sulphone glucoside showed that, generally, methæmoglobin begins to appear when the condition of the patient improves and the cerebro-spinal fluid becomes clear or almost clear. As long as the fluid was turbid the administration of even 25 grammes (100 tablets) during the course of ten days did not produce methæmoglobin. On the other hand, the administration of only 7.5 grammes (30 tablets) during the course of three days produced methæmoglobin bands faintly when the cerebro-spinal fluid was clear.

In no instance were sulphæmoglobin bands observed, denoting that this drug is evidently not so easily decomposed in the body under the conditions of this experiment.

On the appearance of methæmoglobin in the blood the amount of drug administered was reduced or stopped, and no clinical evidence of methæmoglobinæmia or cyanosis was observed in such cases.

In one case, where the administration of the sulphone compound was continued for eight days after the appearance of methæmoglobin a distinct blue discoloration of the nails and shallow hurried breathing was observed. The administration of the drug was stopped and the symptoms immediately cleared up.

The spectroscopic examination of the blood was carried out in collaboration with Mr. P. K. Seshian, M.Sc., and the detailed result is being published as a separate paper which follows this one.

*Treatment with Cepticide.*—When the stock of diaminodiphenyl was running out, a supply of drug named cepticide, manufactured locally, was received for trial and a few cases were treated on similar lines except that cepticide in doses of 3 grammes per day was given instead of the sulphone compound. Cepticide is the trade name of amino-benzene sulphonamide-para, manufactured by the Lister Antiseptics & Dressings Co. It is in tablet form, each tablet containing 0.5 gramme. Two tablets were administered orally three times a day in addition to anti-meningococcal serum. The results obtained are given in table VI.

Gram-negative diplococci resembling meningococci were found by microscopic examination to be present in the cerebro-spinal fluid of all excepting three patients included in the above table. The three exceptions (nos. 77, 86 and 89) proved to be cases of pneumococcal meningitis.



TABLE VI

The results obtained by the treatment of meningococcal and pneumococcal infections with cepticide and anti-meningococcal serum

Case number	Amount of cepticide given (in gm.)	AMOUNT OF SERUM GIVEN (IN C.C.M.)		Result	Days in hospital	Bacteriological examination
		I T	I V			
75	21	100	140	Cured	13	I.
76	12	60	80	Died	5	C.
77	25.5	..	..	Cured	22	Pneumococcal meningitis.
78	2	10	30	Died	$\frac{1}{2}$	Nagg.
79	3	35	60	"	3	C.
80	18	70	140	Cured	8	II.
82	6	30	60	Died	4	N. G.
84	15.5	30	80	Cured	18	N. G.
85	18	40	120	"	20	Nagg.
86	12	..	..	Died	12	Pneumococcal meningitis.
87	15	60	145	Cured	14	N. G.
88	21	70	140	"	29	C.
89	6	..	..	Died	2	Pneumococcal meningitis.

Of the 13 patients treated with cepticide, ten were meningococcal meningitis infections. The percentage of deaths among these ten was 40 per cent. There were no toxic nor any other untoward symptoms attributable to the drug in any of the 13 cases. Three were pneumococcal infections two of which proved fatal.

Hewell and Mitchell (1939) report that three of six pneumococcal meningitis patients recovered when treated with sulphanilamide and related compounds, whereas the mortality rate was 100 per cent among 23 cases treated during 10 years prior to the introduction of these chemotherapeutic drugs. During the course of this investigation, among 91 cases of meningitis examined, ten were found to be pneumococcal infections. All the ten cases were treated with chemotherapeutic drugs (seven with the diamino compound and three with cepticide) and none of them received anti-pneumococcal serum. Nine of these ten died so that one at least of the two drugs used had no beneficial action in the treatment of this disease under the conditions of the experiment employed.

There are obviously a fair number of cases of pneumococcal meningitis admitted to the Campbell Hospital. We are not aware if these were diagnosed previously, but we would recommend that provision of anti-pneumococcal serum be made for the treatment of these cases. The introduction of M. & B. 693, which is said to be almost specific for certain pneumococcal infections, may provide a valuable and relatively cheap mode of treatment, nevertheless it is felt that even with M. & B. 693, anti-pneumococcal serum will be required and should be provided.

**Bacteriological examination.**—Cerebro-spinal fluid from 91 cases admitted to the meningitis ward was examined bacteriologically. A 37°C.

incubator was kept in the ward in which tubes containing 1 per cent pigeon-blood agar were placed a day previous to being used. These tubes were inoculated directly at the bedside when lumbar puncture was done. About 10 drops of cerebro-spinal fluid was allowed to fall into the pigeon-blood-agar tubes after allowing the first few drops to drain away. The tubes were immediately replaced in the incubator. More cerebro-spinal fluid was caught in sterile test-tubes. A portion of the fluid was centrifuged and the deposit examined microscopically and seeded on to another pigeon-blood-agar slope.

Microscopical examination was done by making films of the deposit and staining according to Gram's method.

By microscopic examination ten were found to be pneumococcal infections, 76 showed Gram-negative diplococci resembling meningococci, and five showed no organisms and no pus cells. Pneumococci were isolated from all the ten cases by inoculating 1 c.cm. of the cerebro-spinal fluid intraperitoneally into a mouse and recovering the organism from the heart blood, when the inoculated animals died next morning.

The isolation of meningococci proved more difficult. In only 39 of the 76 cases were meningococci isolated; 15 were contaminated and two were not cultured so that meningococci were isolated from 39 out of 59 cases (66 per cent). The inoculated tubes were examined daily for four days. Those showing a growth were stained by Gram's method and verified to be Gram-negative diplococci; they were next inoculated into serum water, containing either lactose, glucose, maltose or saccharose and an indicator; all the 39 behaved like meningococci in that they fermented glucose and maltose. The agglutination test was next done employing groups I and II meningococcal agglutinating serum obtained from Dr. Gardner of the Standards Laboratory, Oxford. The most frequent contaminants were *Staphylococcus albus* and *Nisseria catarrhalis*; two or more contaminating organisms were usually present together. The following summarizes the bacteriological findings:—

Total number of cases examined culturally .. .. .	89.
Number of cases in which the cerebro-spinal fluid showed no growth on pigeon-blood agar .. .. .	25
Number of cases in which pneumococci were isolated .. .. .	10
Number of cases in which meningococci were isolated:—	
Group I meningococci .. .. .	18
" II " .. .. .	10
Meningococci not agglutinable .. .. .	11
	39
Number of cases in which the cerebro-spinal fluid proved to be grossly contaminated .. .. .	15

(Continued at foot of opposite page)

# SPECTROPHOTOMETRIC EXAMINATION OF BLOOD IN THE TREATMENT OF MENINGITIS WITH DIAMINODIPHENYL-SULPHONE GLUCOSIDE

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AMONG the modern triumphs of chemotherapeutic researches, the administration of sulphanilamide and several other derivatives of aromatic compounds containing both sulphur and amino groups for streptococcal infection is the most striking. Because of the great efficiency of the drug there has sometimes been uncontrolled administration in large doses which has produced toxic symptoms. In several cases marked cyanosis has occurred, which is one of the clinical symptoms of toxicity. The cyanosis following the adminis-

(Continued from previous page)

## Summary

1. The mortality rate among 34 cases of meningococcal meningitis treated with diaminodiphenyl-sulphone glucoside, either alone or together with anti-meningococcal serum, was 32.35 per cent.

The mortality rate in similar series of 32 cases treated with anti-meningococcal serum alone was 60 per cent.

2. The mortality rate was 41.7 per cent when 12 meningococcal meningitis cases were treated with the sulphone compound without administration of anti-meningococcal serum and fell to 27.3 per cent in a second series of 22 meningococcal cases treated with both anti-meningococcal serum and drug. The rate for a corresponding series of cases treated with anti-meningococcal serum was 75 per cent and 60 per cent, among 12 and 20 cases.

3. Diaminodiphenyl-sulphone glucoside, under the conditions of this experiment, appears to be of little value in the treatment of pneumococcal meningitis.

4. Cepticide was administered to ten meningococcal and three pneumococcal meningitis cases. The drug was non-toxic in the doses employed. The mortality rate in the cepticide series was 40 per cent, while that obtaining in the control series was 60 per cent. The number is too small to warrant the drawing of conclusions.

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tration of prontosil has been recently found to be due to the appearance of methæmoglobinæmia or sulphæmoglobinæmia or both in the blood. Brownlee (1939) has observed that the presence of aromatic amino groups causes derangement of the pigment metabolism and produces the toxic symptoms which often follow the administration of drugs containing the amino group.

Spectroscopic examination of the blood of patients provides an efficient technique for the study of the mechanism of cyanosis, and helps to identify the various pigments present in the blood. Discombe (1937), Paton and Eaton (1937) and others have studied the appearance of methæmoglobinæmia and sulphæmoglobinæmia in patients receiving sulphanilamide orally with and without magnesium sulphate or hydrochloric acid. They have recorded that the spectroscopic examination was the most sensitive and reliable method of diagnosis. Colebrook and Kenny (1936), and Colebrook and Purdie (1937) in a study of the treatment of puerperal fever by sulphanilamide examined the absorption spectra of the blood of 60 cyanosed patients and found 24 cases of sulphæmoglobinæmia, 13 cases of methæmoglobinæmia and 8 cases of both. Recently, Welb and Kniakzuk (1939) have made a spectrophotometric examination of the blood of rats receiving sulphanilamide and have observed methæmoglobin and sulphæmoglobin in the blood after its prolonged administration. Several other workers have recorded that the spectroscopic examination of the blood was several times more sensitive than the clinical diagnosis, and alone was able to decide whether the cyanosis was due to methæmoglobin, sulphæmoglobin or both, or to some other pigments. Such an observation is extremely important in researches on chemotherapeutic studies of organic compounds, as the formation of sulphæmoglobin may be due to the reaction of the decomposition products of the drug in the blood. Sulphæmoglobin being a more stable derivative of hæmoglobin is eliminated from the system only slowly and with difficulty.

We have been carrying out investigations on the chemotherapy of diaminodiphenyl-sulphone glucoside for meningococcal infection in patients admitted in the Campbell Hospital, Calcutta. Buttle and co-workers (1937) have observed in animal experiments the presence of methæmoglobin in the blood after the administration of the drug. The opportunity for using the spectroscopic examination of the blood was utilized for controlling the administration of the drug and stopping it as soon as the methæmoglobin absorption band was observed. In this paper some of the observations on the appearance of the absorption bands of the blood are discussed.

It is well known that each of the hæmoglobin derivatives has a specific absorption spectrum in the visible region which helps considerably

in the identification and estimation. Oxy-hæmoglobin has bands, known as  $\alpha$  and  $\beta$ , at  $570\text{ m}\mu$  and  $530\text{ m}\mu$  while that of carboxy hæmoglobin are at  $560\text{ m}\mu$  and  $525\text{ m}\mu$ . The difference in the position of the absorption bands are used for the detection of carbon-monoxide poisoning. The distance between the two bands is known as the 'span'. Measurements of the intensity of the absorption at  $540\text{ m}\mu$  of the blood solution after the addition of  $\text{K}_3\text{Fe}(\text{CN})_6$  and KCN are used by Drabkin and Austin (1935) for the spectrophotometric estimation of hæmoglobin. The bands of methæmoglobin



Fig.1.

Negative



Fig.2.

Faint



Fig.3.

Intense



Fig.4.

Very Intense

↓ MHB  
↓  $\text{d}\alpha\text{HbO}_2$   
↓  $\beta\text{HbO}_2$   
↓ Bilirubin

and sulphæmoglobin are on the longer wave-length of  $600\text{ m}\mu$  while that of oxy, carboxy, cyano derivatives of hæmoglobin are on the shorter wave-lengths of  $600\text{ m}\mu$ . Sulphæmoglobin has an absorption band between  $615\text{ m}\mu$  and  $625\text{ m}\mu$  with a maximum at  $620\text{ m}\mu$ , while that of methæmoglobin is between  $625\text{ m}\mu$  and  $635\text{ m}\mu$  with a maximum at  $630\text{ m}\mu$ . Moreover on addition of a drop of ammonium sulphide or ammonia to the solution, the band at  $630\text{ m}\mu$  due to methæmoglobin disappears, and the band at  $620\text{ m}\mu$  of sulphæmoglobin persists. This is used as a very sensitive test for differentiating between these two derivatives.

In all the experiments 0.2 c.cm. of the oxalated blood were taken, and the erythro-

cyles washed with saline (isotonic) solution twice, and centrifuged. The erythrocytes were hæmolyzed by the addition of 10 c.cm. of distilled water and again centrifuged. The clear solution was poured into a Baly's absorption tube where the length of the absorbing column could be altered from 1 mm. to 100 mm. The absorption bands were observed through a direct-vision spectroscope and photographed on a panchromatic plate with a Zeiss spectrograph of dispersion 90 Å per mm. at  $520\text{ m}\mu$ . A tungsten-filament lamp with quartz window taking 6 amps. (Zeiss) served as the source of light in the visible region. If the absorption bands at  $630\text{ m}\mu$  could be observed with a 40 mm. column it was marked as very intense, 60 mm. as intense, and 80 mm. as faint. If it could be observed only with a 100 mm. column it was marked as very faint and if it could not be observed even with a 100 mm. as negative. This gives a rough indication of the quantity of the pigments contained therein. In every case a drop of ammonium sulphide was added to observe the behaviour of the band at  $630\text{ m}\mu$ . In all cases the band disappeared completely, indicating that it was due to methæmoglobin and not to sulphæmoglobin. In figures 1 to 4 are given photographs of the absorption bands exhibiting negative, faint, intense and very intense bands of methæmoglobin.

In the following table the observation of methæmoglobin in the blood of patients with meningitis treated with the diaminodiphenylsulphone glucoside (oral administration in the form of tablets 0.25 gr. each) are given. Only one case was pneumococcal and the rest were all meningococcal. The appearance of the cerebro-spinal fluid is given to indicate the progress of the treatment. The total amount of the drug (the number of tablets) consumed on the date marked is also given along with the daily dose.

From the study of the table it will be seen that the methæmoglobin band appears in some cases after as few as 28 tablets (7 gm.) while in others it is absent even after 100 tablets (25 gm.). The patients were all of medium stature and physique and of average weight.

A very striking observation is that usually the methæmoglobin appears in the body only after the cerebro-spinal fluid becomes clear. As long as the fluid is turbid the administration of even 100 tablets (25 gm.) does not produce methæmoglobin. In case 9 even though 132 tablets (33 gm.) were administered the methæmoglobin band was only faint, the condition of the fluid being still hazy. On the other hand the administration of 30 tablets (7.5 gm.) had produced the appearance of the methæmoglobin band faintly in cases where the cerebro-spinal fluid was clear. Thus, it seems that the toxic symptoms begin to appear only after the infection has been removed. In none of the cases was the presence of sulphæmoglobin

observed showing that this drug is evidently not so easily decomposed in the system.

Since in almost every case the administration of the drug was stopped when the spectroscopic examination revealed the presence of methæmoglobin, none of the patients developed cyanosis or any other toxic symptoms. Since the drug treatment was stopped and the

patients were discharged soon after the fluid was clear, it was not possible to observe the time taken for the complete disappearance of methæmoglobin, or the appearance of cyanosis if the treatment had been continued. In one case it was observed that the blood showed no methæmoglobin band the day following the stoppage of the drug though it had been present

TABLE

Serial number	Particulars of patients	Date	Daily total	Number of drug tablets given	Appearance of C. S. F.	Intensity of Mhb band	REMARKS
1	N. K., 30, H. M.*	15-11-38	4	4	Turbid	Negative	Stopped. Discharged.
		16-11-38	8	12	"	"	
		17-11-38	8	20	"	"	
		18-11-38	8	28	"	V. faint	
		19-11-38	8	36	Sl. turbid	"	
		20-11-38	..	36	Hazy	Negative	
		21-11-38	..	36	Clear	"	
2	B., 28, H. M.	16-11-38	0	0	Turbid	Negative	Died.
		17-11-38	4	4	"	"	
		18-11-38	8	12	"	"	
3	R., 30, H. M.	17-11-38	12	20	Turbid	Negative	Reduced. Stopped.
		18-11-38	12	32	"	V. faint	
		19-11-38	12	44	Sl. turbid	Faint	
		20-11-38	12	48	"	Intense	
		21-11-38	4	52	Clearer	V. intense	
		22-11-38	4	56	Clear	Intense	
4	B. S., 22, H. M.	23-11-38	12	32	Turbid	Negative	Stopped.
		24-11-38	12	44	Sl. turbid	"	
		25-11-38	12	56	"	"	
		26-11-38	12	68	Hazy	V. faint	
		27-11-38	12	80	Clear	Faint	
		28-11-38	12	92	"	Intense	
5	D. D. C., 22, H. M.	23-11-38	12	28	Turbid	Negative	Stopped.
		24-11-38	8	40	Sl. turbid	"	
		25-11-38	8	48	"	"	
		26-11-38	8	56	"	"	
		27-11-38	8	64	Clear	V. faint	
		28-11-38	8	72	"	Faint	
6	R. R., 18, H. M.	8-12-38	8	32	Turbid	Negative	Died.
		9-12-38	8	40	"	"	
		10-12-38	8	48	"	V. V. faint	
		12-12-38	8	64	"	V. faint	
		14-12-38	8	80	"	Faint	
		15-12-38	8	88	"	"	
7	N. S., 26, H. M.	12-12-38	12	14	Turbid	Negative	Died.
		14-12-38	12	38	"	Intense	
		15-12-38	12	50	"	V. intense	
8	A. C. C., 20, H. M.	21-1-39	12	48	Turbid	Negative	
		24-1-39	..	84	"	"	
9	A., 30, H. M.	21-1-39	12	96	Sl. turbid	V. faint	
		24-1-39	12	132	Hazy	Faint	
10	B. S., 25, H. M.	21-1-39	12	84	Turbid	Negative	Stopped.
		24-1-39	..	110	"	V. intense	
11	R. D., 24, H. M.	21-1-39	8	156	Clear	Negative	Discharged.
		24-1-39	..	70	"	V. faint	
12	K. M., 25, H. M.	21-1-39	4	52	Turbid	V. faint	Stopped.
		24-1-39	..	64	"	Intense	

\*H. M. = Hindu male. V. = very. The particulars of the patient given are, initials, age, religion and sex.  
(Continued at foot of next page)

## DIFFERENT SEROLOGICAL RACES OF LEPTOSPIRA IN THE ANDAMANS

By B. M. DAS GUPTA

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THE materials on which this investigation is based were received through the courtesy of Major B. Chaudhuri, I.M.S., senior medical officer, the Andaman and Nicobar Islands, and

(Continued from previous page)

faintly the day previous. In another case where the administration of the sulphone compound was continued for eight days after the appearance of the methæmoglobin band a distinct blue discoloration of the nails and shallow hurried breathing was noted. The administration of the drug was immediately stopped.

The high sensitivity and reliability of this type of spectroscopic diagnosis of methæmoglobinæmia for controlling the administration of sulphur and amino derivatives of aromatic compounds has to be recorded.

It is a pleasure to record our thanks to Dr. G. Sankaran, professor of biochemistry and nutrition of the All-India Institute of Hygiene and Public Health, for helpful suggestions and facilities afforded for the investigation. Most of the expenses for this investigation were defrayed from grants from the Endowment Fund of the Calcutta School of Tropical Medicine.

### Summary

The appearance of the absorption band at 630  $m\mu$  and its behaviour on addition of ammonium sulphide are used as a very sensitive method for detecting the presence of methæmoglobin and sulphæmoglobin in blood.

It is observed that on administration of diaminodiphenyl-sulphone glucoside for meningococcal infection no sulphæmoglobinæmia is produced.

It is also observed that generally methæmoglobin begins to appear on the administration of the drug only after the cerebro-spinal fluid becomes clear.

When the administration of the drug is stopped after the appearance of the methæmoglobin band in the blood, no toxic effects are produced.

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Dr. H. D'Silva, senior assistant surgeon, Port Blair. They consisted of blood cultures on Fletcher's or Vervoot's medium and sera from cases of leptospirosis which occurred in this settlement from August 1938 to April 1939. The specimens which were unsuitable for examination or failed to show significant evidence of leptospiral infection have been left out of account.

As it was shown by Taylor and Goyle (1931), who have carried out a comprehensive and highly efficient investigation into leptospirosis in the Andamans, that there exist in these islands two distinct serological groups, e.g., CH 11 and CH 31, it has been our object to determine to which of these groups the five strains isolated in the settlement during the above period belong. Accordingly anti-sera were prepared against the two strains referred to above by injecting rabbits with rich living cultures in Vervoot's medium. Usually eight injections were necessary for the production of a high-titre agglutinating serum. The immunized rabbits were bled a week or ten days after the last injection and the sera gave a titre of 1:10,000 in both the cases. As one of the strains was not agglutinated by either of the anti-sera it was sent to the Schüffner Laboratory at Amsterdam for the purpose of further investigation, with a view to determining its true serological character.

All the sera obtained on different days of illness were first tested against the two established Andamans strains (CH 11 and CH 31). The specimens which did not yield any definite reaction with the above strains were also sent to Prof. Schüffner for testing against the representatives of several other serological groups.

TABLE I  
Serological grouping of the strains

Anti-sera (1:10,000)	STRAINS				
	Jamsher *	Mg. Tin Tin *	Potin	Sherkhan	No. 4
Andamans CH 11 ..	10,000	..	10,000	10,000	20
Andamans CH 31 ..	10,000	100	..	..	..
Moscou V ..	..	..	..	..	..
Rachmat ..	..	..	..	..	..
Rat (Semarang 173) ..	..	..	..	..	..
H. Utrecht IV ( <i>L. canicola</i> ) ..	..	300	..	..	..
Vleermuis 90C ..	..	10,000	..	..	..
Hebdomadis ..	..	..	..	..	..
Sarmin ..	..	100	..	..	..
Chopra ( <i>L. ictero-hæmorrhagiae</i> ) ..	..	100	..	40	..
Kantorwicz ( <i>L. icter.</i> ) ..	100	1,000	..	..	..
Wijnberg ( <i>L. icter.</i> ) ..	..	300	..	..	..

\* Tests were carried out at the Schüffner Laboratory at Amsterdam.

Moscou V = Andamans CH 31.



TABLE II

Sera showing agglutinative action either on Andamans CH 11 or Andamans CH 31

Number of specimens	STRAINS	
	CH 11	CH 31
74	..	+ 1 : 160 *
2	+ 1 : 20	+ 1 : 160 *
2	+ 1 : 160 *	+ 1 : 20
3	+ 1 : 160 *	..
1	+ 1 : 30	+ 1 : 10,000
1	+ 1 : 10	+ 1 : 3,000
1	+ 1 : 30	+ 1 : 300

\* Higher dilutions not tried.

TABLE III

Sera showing high degree of agglutination with strains other than CH 11 and CH 31

Sera	<i>L. icter.</i>	<i>L. canicol.</i>	CH 11	CH 31	Semarang 173	90 C	Rachmat
Convict no. 7549	300	300	10	..	..	1,000	..
Serum no. 1 ..	100	300	10	..	..	3,000	..
Serum no. 29 ..	10,000	100	10	100	..	..	..
Marquis Beg	10,000	1,000	30	100	..	..	..
Punnu Swamy	100	..	..	10	..	3,000	..

It will be obvious from table I that, out of the five strains isolated, four belong to the same serological group as Andamans CH 31, the remaining one being identical with a Java bat strain (90 C). It should be mentioned here that, according to Prof. Schüffner who is responsible for typing this last-named strain, this is the first time that this type has been recovered from a human case. The sera listed in table II yielded significant positive agglutinations, chiefly with the Andamans CH 31. A few, however, agglutinated Andamans CH 11. It may be recalled that in 1931 Taylor and Goyle noted that out of twenty-eight strains studied by them only four were agglutinated by CH 31 anti-serum and all the rest belonged to the same group as CH 11. Table III shows that three specimens of sera react with 90 C in high dilutions, although a certain amount of co-agglutination was found with some other strains. Two specimens agglutinated the classical strain (*L. icterohæmorrhagiæ*) in a very high dilution (1 : 10,000), thus showing that the organism belonging to the *icterohæmorrhagiæ* group also exists in the settlement, though its occurrence appears to be the least common.

#### Summary

There exist in the Andamans two other serological types of leptospira (Java bat type '90 C' and the classical *L. icterohæmorrhagiæ*)

(Continued at foot of next column)

## TAKING BLOOD FOR TRANSFUSION

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COMPLAINTS are often received from donors of blood, who go out to serve through this laboratory, regarding incisions, large or small, made over a vein, and regarding pain caused by needles of large bore. Comments are also heard regarding the way the blood is exposed during collection. This communication is published with a view to helping those unfamiliar with a less painful and more aseptic technique and thereby adding to the ease and safety of blood transfusion. In it (i) the taking of blood in a solution of sodium citrate, and (ii) defects in the sodium citrate solution will be dealt with.

#### I. Taking of blood in a closed system, under negative pressure, into a solution of 2.5 per cent sodium citrate

Potain's aspirator supplies the system and is too well known to need description. All the parts, except the pump, are sterilized and assembled with aseptic precautions. Into the bottle is put 2.5 per cent sterile sodium citrate solution, 1/10th volume of the intended total. Into the free end of the rubber tube connected with the inlet in the special stopper is inserted a needle from a 20 c.cm. record syringe, with or without adapter. The rubber tube, connected with the exhaust in the special stopper, is knotted upon itself to form two loose knots in its course in order to prevent contamination of the contents of the bottle with micro-organisms, which may be blown in from the pump with the back stroke of the piston.

About 20 strokes of the pump, held and worked by an assistant, suffice to produce the necessary vacuum.

The needle is introduced into a suitable vein in the arm, after the former has been made

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type) besides those already noted by Taylor and Goyle. Andamans B type (CH 31) appears to be responsible for the infection in a large majority of cases during the period of our investigation.

We wish to express our indebtedness to Major B. Chaudhuri, M.B.E., I.M.S., and to Dr. D'Silva, I.M.D., for supplying the materials on which this work is based. We would also record our grateful appreciation of the valuable assistance rendered by Prof. Schüffner and his staff.

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prominent with a tourniquet *which does not stop the pulse*. No local anaesthesia is necessary. The stopcock connecting the inlet with the bottle is opened. A steady flow of blood results. The bottle is briskly moved (by the assistant who works the pump) with a circular motion, clock-wise and then counter-clock-wise, to mix the blood with the citrate solution. A few more strokes of the pump and readjustment of the tourniquet may be necessary.

The actual quantities of the citrate solution relative to the total contents of the bottle are: 40 c.cm. for 360 c.cm. of blood, total 400 c.cm.; 30 c.cm. for 270 c.cm. of blood, total 300 c.cm.; 20 c.cm. for 180 c.cm. of blood, total 200 c.cm.; and 10 c.cm. for 90 c.cm. of blood, total 100 c.cm.

Ordinary glass stoppered bottles into which the special rubber stopper fits can be used. Marks to indicate quantities are etched or scratched on them.

After taking the required quantity of blood the inlet is closed. Negative pressure is abolished by admitting air slowly through the knotted tube (hissing sound is avoided). The special stopper is removed and replaced by an ordinary sterilized glass stopper which, together with a part of the neck of the bottle, is wrapped round with sterile cotton-wool, gauze or a paper cap (made by moulding two layers of paper over the stopper and the neck of the bottle which it fits). A sterilized and paraffined cork can be used instead of a glass stopper. The bottle is now ready to be passed on to the operator responsible for the transfusion.

The special stopper of the aspirator is placed in running water as soon as it is disengaged, to free it from blood.

From the bottle of citrated blood, transfusion can be given by a closed system (in a bacteriological sense) by means of a rubber tube and a two-way 20 c.cm. record syringe. The rubber tube is secured in the neck of the bottle with a packing of sterile cotton-wool or gauze (kept dry). An ordinary syringe can be made into a two-way syringe by an adapter (cost Rs. 4). Over the free end of the rubber tube in the bottle are tied two layers of fine muslin of good quality (free from loose fibres) to filter out coagula that might have formed before the mixture of the blood with the citrate solution became uniform.

It is considered that for giving citrated blood the usefulness of the improvisation described almost equals that of the apparatus specially designed, including the recently described rotary pump (Riddell, 1939). Potain's aspirator is available in most small dispensaries, far below the class of a district hospital, in India. The parts, of which more than one may be required, are cheap (a spare special stopper cost in Calcutta, Rs. 12 on 3rd October, 1939).

Incidentally, blood letting for other purposes can also be done neatly and quickly by the use

of the same device, sterility being limited to the needle (and to the rubber tube carrying it if no adapter is used) and citrate solution being absent.

## II. Defects in sodium citrate solution

The opinion has steadily gained ground that the 'reactions' attributed to sodium citrate are really due either to incompatibilities of bloods, impurities in the distilled water used, or impurities in the salt itself.

Incompatibilities of bloods have been described by the writers, at length, in a recent communication (Greval and Chandra, 1939). The facts not yet generally recognized are: (i) all group-O subjects are not universal donors, (ii) there are slowly-reacting red cells of group A, (iii) all donors will not suit a group-AB recipient, (iv) a donor may not be compatible for a repeated transfusion, (v) a naturally occurring anti-M substance may be present in the donor or the recipient as an *abnormality*, and (vi) substances other than isohæmagglutinogens A and B or hæmagglutinogens M and N may be responsible for incompatibility. Donor and recipient must belong to the same group and *direct matching must be done*. Recipients AB must be transfused from *safe donors* of other groups if donors AB are not available. In emergencies when grouping is not possible *only safe group-O donors should be used*.

For excluding impurities in water only distilled water from a reliable still should be used.

For excluding impurities in the salt heed should be paid to its chemistry rather than its price. It is surprising how many defects may exist in this simple salt. According to the *British Pharmacopæia* (1932) they consist of (i) undue alkalinity or acidity, (ii) tartrates, (iii) oxalates, (iv) sodium chloride, (v) sulphates, (vi) arsenic and (vii) lead. The *purity of the salt is specially stressed* because of the present shortage of its supply from certain sources. The shortage is likely to increase in the near future.

The writers sterilize their 2.5 per cent solution in a steamer, at atmospheric pressure, for 25 minutes daily, on three consecutive days, usually in quantities given above, in bottles into which the special stopper fits but which are plugged with cotton-wool. Glass stoppers (fitting the bottles) loosely wrapped in paper caps are sterilized at the same time. After sterilization is complete, the cotton plugs are replaced by glass stoppers and paper caps. The bottles are stored in a dust-free receptacle until required. The solution is also sterilized and kept in large test tubes left in an air-tight glass jar. It is poured into an empty sterile bottle when needed.

Highly concentrated sterile sodium citrate solution is put up in ampoules by commercial

(Continued at foot of opposite page)

## ELECTROCARDIOGRAPHY IN THE DIAGNOSIS OF SILENT HEART DISEASES

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THE diagnosis of heart disease is often made more or less accurately by careful history taking and a thorough physical examination. The usual symptoms suggestive of cardiac dysfunction are breathlessness on accustomed exertion, precordial pain, palpitation, and syncope. Their presence, however, is not always pathognomonic of heart disease. Breathlessness on exertion may be present in obesity, emphysema, pulmonary and mediastinal neoplasms, and neuro-circulatory asthenia. Besides, some patients may not be actually conscious of its presence while others (particularly women) may exaggerate it. Thus, it is sometimes difficult to evaluate this symptom.

Precordial pain that is not strictly retrosternal and definitely related to effort may be due to neuro-circulatory asthenia, intercostal panniculitis and fibrositis, gastric and cholecystic disturbances and other causes not related

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firms. Directions regarding quantities are supplied with the ampoules. The writers have no experience of the solution.

In the maximum volume for transfusion, 400 c.cm. for an adult, recommended by the writers, the total quantity of the sodium citrate injected into the recipient is what is contained in 40 c.cm. of a 2.5 per cent solution, i.e.,  $\frac{40 \times 2.5}{100}$  grammes = 1 gramme. Even if the volume were doubled the quantity would only be 2 grammes which is much below the limit of 5 grammes allowed by Lewisohn (Wiener, 1935) who studied in detail the citrating of blood for transfusion.

#### Summary

1. Potain's aspirator can be used in taking blood for transfusion. It can also be used, incidentally, in blood letting.

2. Many defects can exist in sodium citrate. The pure salt under a certain quantity is quite safe for use in citrating blood for transfusion.

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to the heart. Palpitation alone is unreliable as a symptom of heart disease. It is the manifestation of a rapid, forcible or irregular heart action. Digestive disturbances and patient's own sensitivity are often important factors in the production of this symptom. However, it must be remembered that the sudden onset of palpitation on accustomed exertion in middle-aged persons is usually significant of cardiac disease. Syncope is more often a symptom of an unstable vasomotor centre associated with increased vagal tone than of cardiac disease, though it is true that complete or partial heart block, paroxysmal tachycardia, and aortic incompetence may at times be responsible for the symptom.

The usual physical signs indicative of heart disease are cardiac enlargement, alteration of heart sounds, organic murmurs, serious irregularities of rhythm and evidence of cardiac failure. There are cases, however, where the elicitation of some or all of these signs is very difficult, if not impossible. The estimation of the size of the heart in an obese or emphysematous individual is almost impossible. The heart sounds may also be muffled in such subjects. In other cases, as in effort angina, the physical signs are vague and indefinite.

We propose to include under the designation of silent heart diseases all those cases which do not show the usual signs and symptoms of cardiac trouble when they first come under observation, but in which later on strenuous situations or sudden cardiac catastrophes make the disease too apparent. Recognition of the disease in the silent phase will prevent many a calamity of advanced cardiac lesion. Undoubtedly, the electrocardiograph can play an important rôle in the early recognition of such potentially dangerous cardiac disorders.

The so-called silent disorders of the heart may be considered under two groups, (a) toxic and infective, and (b) degenerative.

The chief feature of all these groups is myocardial dysfunction or damage. For an accurate assessment of the myocardial condition an electro-cardiographic examination is as essential as auscultation in the detection of valvular lesions. But the functional or structural changes in the myocardium would often produce similar types of abnormal waves in the electrocardiogram, and thus present difficulties in their proper interpretation, unless the history and the age of the patient are taken into consideration and subsequent follow-up electrocardiograms are taken at suitable intervals. Reversible changes (those due to toxins, drugs, or anæmia) may thus be differentiated from irreversible changes (necrosis and progressive fibrosis due to gradual ischæmia).

#### (a) Toxic and infective groups

*Toxæmia of acute infections.*—In acute infectious diseases such as diphtheria, pneumonia,



typhoid fever and influenza there is diffuse cardiac damage consisting of hyaline changes, fatty degeneration, fragmentation of the muscle fibres and occasionally of small hæmorrhages. The myocardial condition cannot in many cases be judged clinically because definite signs and symptoms are often lacking. On the other hand, symptoms of myocardial weakness may be present, as during convalescence from influenza, although they are really due to neuro-circulatory asthenia. For these reasons, electrocardiographic studies are very helpful in detecting the presence of actual myocardial involvement. Diffuse myocarditis, varying grades of partial heart block, complete heart block, bundle branch block or arborization block may all be detected from the electrocardiogram in otherwise unsuspected cases.

The electrocardiographic abnormalities consist of low-voltage waves in all the leads, flattened iso-electric or inverted T waves, especially in leads I and II, prolongation of the P-R interval beyond the normal limit of 0.2 second, with or without a dropped ventricular complex, and notching of the QRS complex with widening beyond the normal limit of 0.1 second. In this connection it must be emphasized that too much importance should not be attached to low voltage alone in the diagnosis of myocardial damage, because it is a transient change and its absence does not exclude the possibility of myocardial damage. Electrocardiographic tracings, demonstrating myocardial damage in the course of acute infections, are shown in figures 1 to 3.

*Fig. 1.*—This is an electrocardiogram taken on the 15th day of illness in the case of a girl aged 6 years, admitted to hospital with diphtheria on the 8th day of the disease. Physical examination did not reveal any abnormality of the heart. Heart rate, 109 per minute; rhythm regular; P-R interval 0.2 second; T and P waves superimposed; QRS complex thickened and notched in all leads and its duration prolonged to 0.12 second. There is left axis deviation; the ST segment is depressed in leads I and II and iso-electric in lead III. These changes are indicative of left bundle branch block.

*Fig. 2.*—This is the electrocardiogram of a patient, aged 18 years, taken while he was convalescing from influenza. He came in with a history of continuous fever for seven days associated with intense headache, marked generalized pain all over the body, frequent vomiting, and catarrh of the upper respiratory tract. The electrocardiogram was taken on the 8th day of convalescence. On physical examination, no abnormality was detected in the cardiovascular system except a low blood pressure, 90/60 mm. of Hg. Sinus mechanism normal; heart rate 68 per minute; rhythm regular; P pronounced in leads II and III; P-R interval 0.22 (delayed conduction); Q prominent in lead III; right axis deviation; QRS complex markedly notched in lead III; T wave diphasic in lead III; ST segment elevated. The above changes suggest toxic myocarditis.

*Fig. 3.*—Electrocardiogram of a man aged 26 years suffering from typhoid fever of 14 days' duration. The heart was normal in size, but the first sound was faint. The pulse was regular with a rate of 100 per minute. Blood pressure was 100/60 mm. of Hg. Urine examination showed a trace of albumin and a few pus cells. The electrocardiogram shows a picture of diffuse toxic myocarditis. QRS complexes thickened and of poor voltage in all leads; T waves flattened in leads I and

II and iso-electric in lead III; ST segment slightly elevated in lead I.

*Toxæmia due to focal sepsis.*—Long continued absorption of toxins from various septic foci such as tonsils, teeth, nasal sinuses, diseased gall-bladder and prostate may not only aggravate pre-existing heart disease, but may also give rise to cardiac disturbances in apparently healthy individuals. It is often difficult to ascertain clinically how far the cardiac symptoms are purely functional in nature and how far they are due to an underlying myocardial lesion.

*Fig. 4.*—Electrocardiogram of a man, aged 38 years, who gave a history of recurrent attacks of maxillary sinusitis. Clinical examination did not reveal any abnormality in the heart; heart rate 93 per minute; rhythm regular; QRS complexes notched and splintered, timing 0.11 second (prolonged); T waves in leads I and II flattened and iso-electric in lead III. This picture is indicative of myocarditis with delayed intraventricular conduction.

*Thyrotoxicosis.*—Apart from acceleration of the heart beat due to increased basal metabolism, thyroxin appears to act directly upon the myocardium causing tachycardia and even auricular flutter and fibrillation. Histopathological changes in the heart are difficult to demonstrate, but occasionally patchy degeneration, round-cell infiltration, and fibrosis may occur. Electrocardiogram shows very often unusually large P waves, high T waves, depression of ST segments or inversion of T waves, particularly after digitalization. One of our patients a female, aged 38 years, who came under observation lately, had all the usual symptoms and signs of thyrotoxicosis. Her pulse rate was 120 per minute, and blood pressure 130/85 mm. of Hg. Her lungs were slightly emphysematous. Examination of the heart did not reveal any abnormality apart from the increased rate, but electrocardiogram revealed definite evidence of toxic myocarditis.

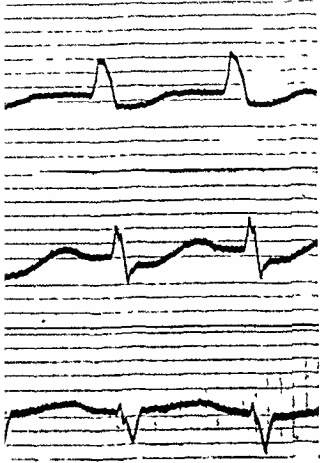
*Obstructive jaundice.*—In chronic obstructive jaundice the retained bile salts exert a toxic influence on the myocardium causing cloudy swelling, granular degeneration and fatty changes in the muscle fibres. When the patient is examined, evidence of the above changes in the muscles can rarely be detected, but an electrocardiographic examination often shows that the myocardium is damaged.

The following case may serve as an illustration:—

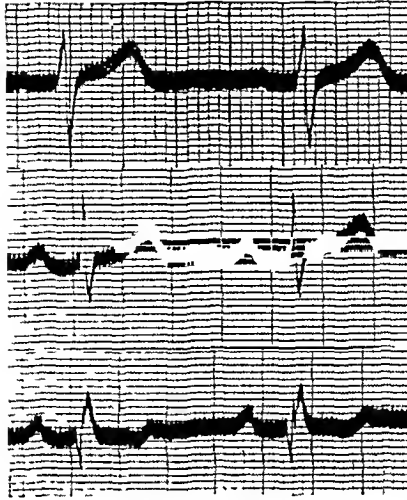
*Fig. 5* is an electrocardiogram of an Anglo-Indian female, aged 28 years, suffering from obstructive jaundice for the last year and a half. She had a big liver, which was somewhat firm in consistency and slightly tender. Her stool contained very little bile and her van den Bergh reaction was immediate direct positive with a bilirubin content of nine units. Her general condition was fairly good, but her electrocardiogram showed marked toxic myocarditis.

*Epidemic dropsy.*—In Bengal this malady must be considered as a serious problem; and many deaths occur every year during the epidemic outbreaks in different parts of the

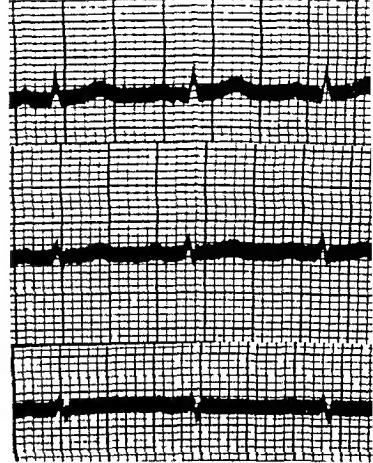
PLATE I



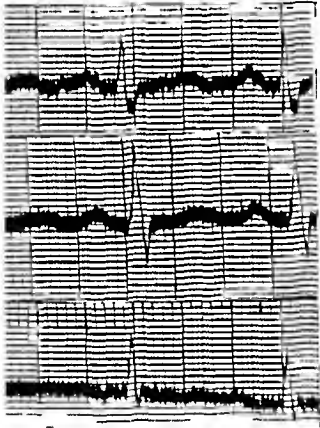
Case 1.



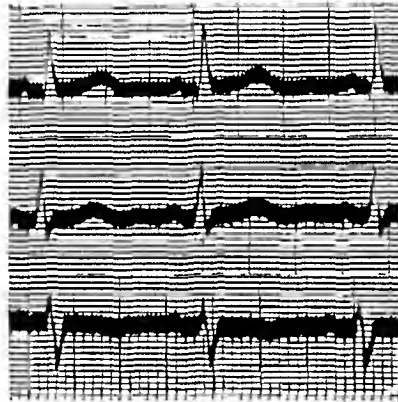
Case 2.



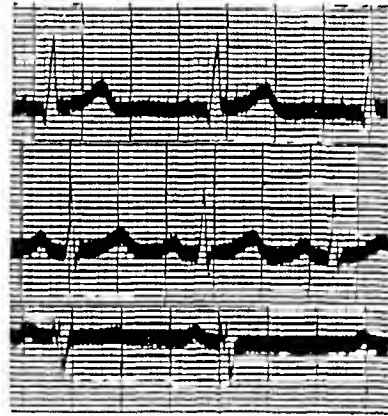
Case 3.



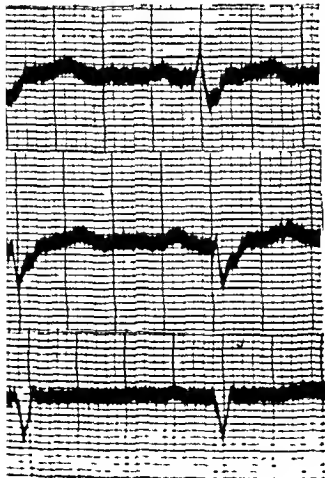
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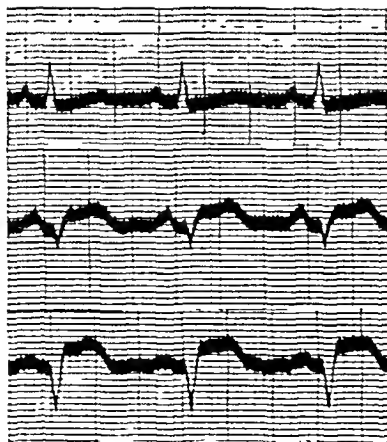
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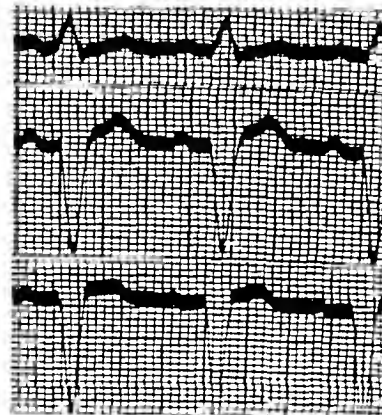
Case 6.



Case 7.

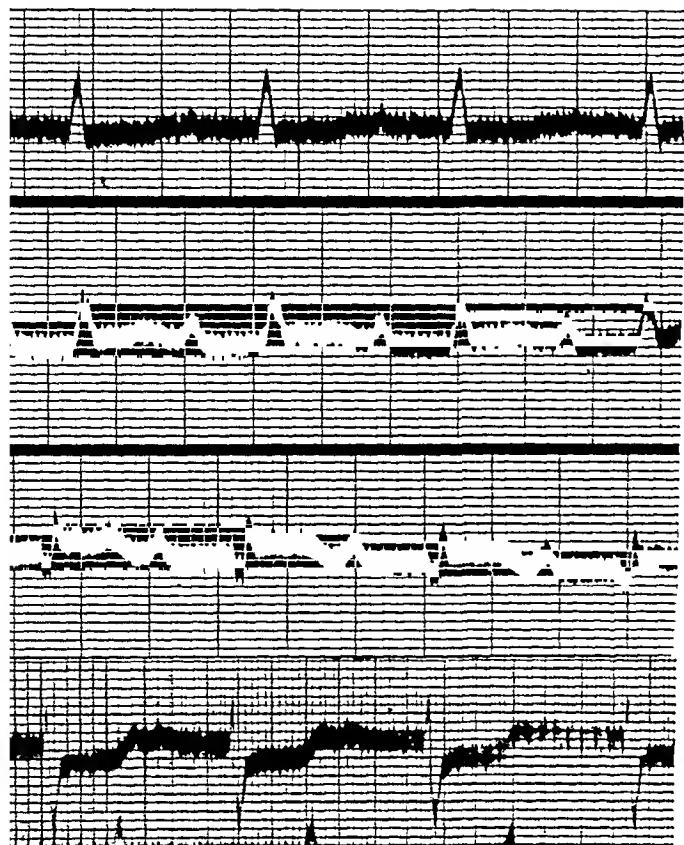


Case 8.



Case 9.

# PLATE II

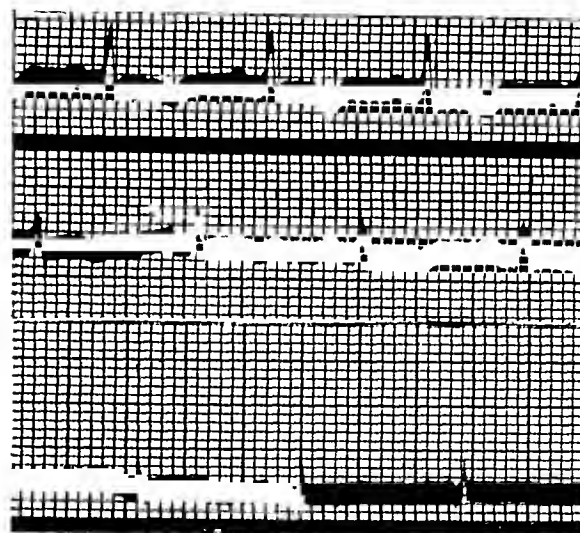


Case 10.

Lead  
I

II

III



Case 11.

Lead  
I

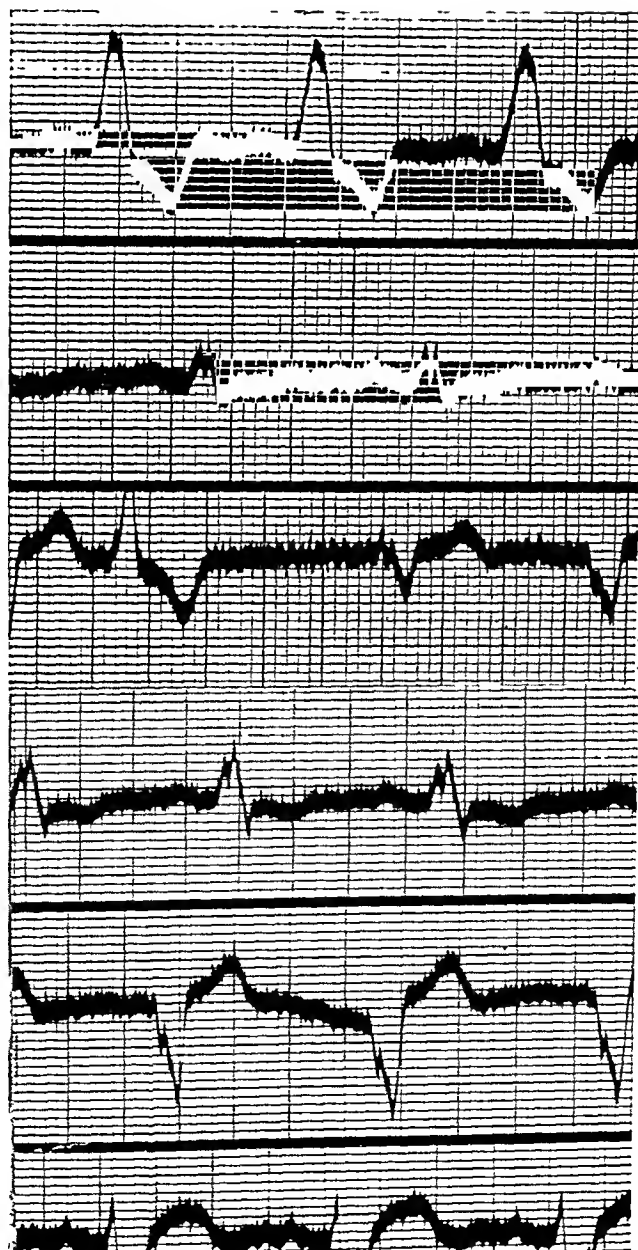
II

III

II  
Extension

III  
Extension

IV



country. One of the common causes of death in this disease is sudden cardiac failure. On many occasions, when the heart is examined clinically, it appears to be normal and yet it is in these cases that death may occur subsequently from acute myocardial failure. To forestall such a catastrophe it is essential to assess the myocardial conditions and one of the surest methods to do this would be to make an electrocardiographic examination.

Fig. 6 shows the picture of the heart of a young man of 23 years, who had been suffering from occasional palpitation since an attack of epidemic dropsy two years ago. The patient looked apparently well and no abnormality could be detected in the heart by physical examination, except that the rate was rapid, but an electrocardiographic examination showed definite evidence of a toxic myocarditis.

### (b) Degenerative group

The occurrence of degenerative changes in the coronary arteries, gradually leading to a focal or diffuse ischaemic myocardial fibrosis, may be to a certain extent a physiological event from the age of forty-five onwards, but it is encountered more markedly and more frequently in persons who suffer from hypertension, diabetes mellitus, myxoedema, or gout. Heredity is also an important factor. The coronary disease, which is in most cases of an atheromatous nature and which in many cases manifests itself clinically by effort angina, may remain entirely asymptomatic for some time before congestive failure ensues, or the more serious disaster of coronary thrombosis occurs. The electrocardiographic studies made during this silent phase may help us a good deal in estimating the condition of the coronary circulation and the degree of myocardial damage consequent to such ischaemia. Even when the symptoms of effort angina are present, they are not necessarily due to coronary disease, for they may be present in severe anaemia and thyrotoxicosis. Hence in such circumstances, too, the electrocardiographic studies become essential. The changes in the electrocardiogram usually consist of prominent Q 3, widened and bizarre QRS complex, deformed ST segment, and iso-electric, inverted or diphasic T waves, particularly in leads I and II. The use of the fourth lead (precordial lead) may be of advantage because in 17 per cent of cases the changes suggestive of myocardial damage and coronary disease are found in this lead alone (Bourne and Evans, 1938). In one-third of the cases, however, electrocardiographic studies fail to show any abnormality in spite of the use of the precordial lead.

When coronary thrombosis occurs, it usually manifests itself with such symptoms and signs as to enable the physician to arrive at a diagnosis with sufficient accuracy. But sometimes atypical symptoms may mislead one to

the diagnosis of acute abdominal catastrophe, bronchial asthma and even uraemia. Unless investigations are made with the electrocardiograph, the underlying disease will be overlooked and the treatment will be directed on wrong lines. Here are some electrocardiograms which illustrate the above-mentioned peculiarities of the coronary heart disease.

Fig. 7.—Male, aged 65, came in with the complaint of thumping inside the chest and a dull pain in the precordium. On physical examination, no abnormality was detected. Blood pressure was 120/80 mm. of Hg. The electrocardiogram shows—left ventricular preponderance, comparatively small excursions in all the leads, ventricular complexes widened to 0.16 second, notched and slurred. Advanced myocardial degeneration with intra-ventricular block is indicated.

Fig. 8.—Male, aged 53, came in with the complaint of severe pain in the left half of the upper abdomen and the lower part of the left side of the chest. He also vomited several times at the onset of the pain, which was thought by his family physician to be of gastric origin, and treated accordingly with gastric sedatives and gavage, without appreciable relief. On examination, pulse rate was 124 per minute, rhythm regular. Blood pressure 120/85 mm. of Hg. Heart sounds were feeble. There were no other physical signs of importance. On enquiry, the patient gave no history of previous attacks of dyspnoea or angina. The electrocardiogram showed coronary thrombosis.

Fig. 9.—Male, aged 72 years, came in with the complaint of oliguria for one week and anorexia for one month. Heart sounds were feeble. Rate was 100 per minute and rhythm regular. Blood pressure 100/60 mm. of Hg. Superficial arteries were markedly thickened. Urine showed a trace of albumin. The electrocardiogram showed left bundle branch block (new nomenclature) and coronary insufficiency.

Fig. 10.—Male, aged 70 years, came in with the complaint of sudden griping pain all over the abdomen and frequent vomiting followed by some breathlessness. Heart sounds were feeble, rate 100 per minute, regular. Blood pressure 90/60 mm. of Hg. Arteries were thickened. Lungs emphysematous. Urine examination revealed leucocytosis (17,160 per c.mm.) of the polymorphonuclear type (82 per cent). Urine showed trace of albumin and a few hyaline and granular casts. The electrocardiogram showed P-R interval 0.22 second; QRS grossly notched in all the leads; T deformed in all the leads; ST marked 'high take off' in lead III; also depressed in I and deformed in II. Chest lead confirmed presence of coronary thrombosis.

Fig. 11.—Male, aged 43, came in with the complaints of headache, insomnia and haziness of vision for ten days. He gave a history of suffering from diabetes mellitus and high blood pressure for the last two years. On examination, his blood pressure was found to be 240/150 mm. of Hg. Arteries were markedly thickened. No abnormality in the heart could be detected by physical examination. Urine showed the presence of sugar and albumin. The electrocardiogram showed marked myocardial degeneration with coronary sclerosis.

Fig. 12.—Male, aged 63 years, came in with the complaint of giddiness and breathlessness on accustomed exertion for one year. Occasionally, he used to get a mild sub-mammary pain on the left side with no definite radiation. Blood pressure was 175/100 mm. of Hg. Arteries were markedly thickened. Pulse rate 82 per minute and irregular due to extra-systoles. No abnormality was detected in the heart except the extra-systoles and feeble heart sounds. Lungs were emphysematous. The electrocardiogram showed ventricular extra-systoles, widened and grossly notched QRS with T in the opposite direction in I and III. ST depressed in I and II, elevated in III; evidence of left bundle branch block with coronary sclerosis.

(Continued at foot of next page)

# REPORT OF TWO POST-MORTEMS AND FIVE CASES OF ADDISONIAN PERNICIOUS ANÆMIA

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BECAUSE of the interest taken in macrocytic tropical anæmia in India due to the work of Wills (1931 and 1934), Napier (1936 and 1939) and others, and also because of the occurrence of severe anæmias due to such causes as ankylostomiasis and malaria, the occurrence of true Addisonian pernicious anæmia tends to be overlooked in India. Davidson and Fullerton (1939) in the *Medical Annual* write that 'Pernicious anæmia is apparently comparatively rare in India and the East', while Ungley in the Goulstonian lecture of 1938 said 'Pernicious anæmia is pre-eminently a disease of Europe and North America'.

In the Punjab, true pernicious anæmia is not rare. We give below details of five cases and two post-mortem examinations of cases, recently seen in the medical wards of the Mayo Hospital, Lahore.

**Case 1.**—Hindu, male, aged 60, agriculturist, admitted on 25th November, 1937.

**Complaints.**—Six months' weakness and swelling of the whole body.

**Condition on admission.**—Puffiness of face, no wasting of abdomen or limbs which were still covered with ample fat. The colour of the skin was typically lemon-tinted. The muscles were flabby. There was no history of diarrhœa or soreness of the tongue. He had lived on an ample Punjabi diet. There was no history of malaria.

**Examinations.**—Heart slightly enlarged; apex beat in the 6th intercostal space; systolic murmur in the pulmonary area and marked *bruit-de-diable*.

Spleen and liver not palpable. Teeth, no marked pyorrhœa, tongue normal, no superficial glossitis.

(Continued from previous page)

## Summary

1. The occasional difficulties in the diagnosis of heart disease unaided by the electrocardiograph have been pointed out.

2. The value of electrocardiography in diagnosing silent phases of serious cardiac disorders has been stressed.

3. Illustrative electrocardiograms have been appended.

We wish to express our sincere thanks to Lieut.-Colonel J. C. De, I.M.S., Superintendent, Medical College Hospitals, for permission to publish the case records, to Lieut.-Colonel E. H. Vere Hodge, I.M.S., for the records in connection with figures 1, 4, 6 and 7, and to Mr. A. C. Sinha for his technical help.

## REFERENCE

Bourne, G., and Evans, C. (1938). *Lancet*, ii, p. 1354.

There was no sign of nervous disease: reflexes and sensation normal.

## Blood examination—

Date	Total red cells in 10 <sup>6</sup> per c.mm.	Hæmoglobin, per cent	Size of red cells, $\mu$	Reticulocyte count, per cent.
26-11-37	1.10	25	8.0	2
5-12-37	1.50	35	8.1	46
14-12-37	2.50	55	..	10
20-12-37	3.50	65	..	8
1-1-38	3.75	75	..	5
6-1-38	3.80	80	..	3
20-1-38	4.10	80	..	3
29-1-38	4.25	80	..	2
28-2-38	5.00	95	..	2

The leucocyte count was 3,000 per c.mm. on admission and no nucleated red cells were seen; anisocytosis and poikilocytosis were very marked.

The van den Bergh reaction was indirect positive.

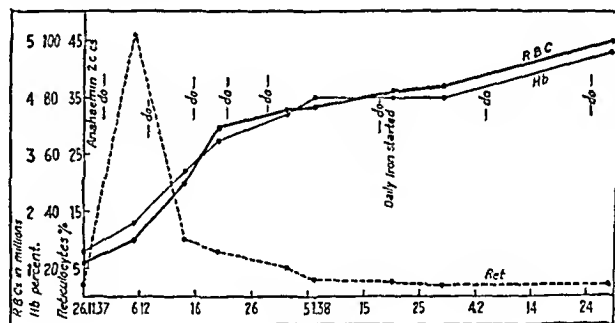
**Gastric analysis.**—No free hydrochloric acid after porridge meal or histamin injection.

**Stool examination.**—Negative for ova, cysts and amœbæ.

**Sternal puncture.**—Rare megaloblasts and a few normoblasts.

The diagnosis of pernicious anæmia was tentatively made in spite of the absence of nucleated red cells in the peripheral circulation.

He was given anahæmin (B. D. H.) 2 c.cm., intramuscularly, three times in the first fortnight and then at weekly intervals.



Case 1.

There was a typical reticulocyte response after six days, when the reticulocyte count rose to 46 per cent. The accompanying chart shows the changes in the blood picture (case 1). In two months the hæmoglobin had risen to over 80 per cent and red cell count to 4,000,000. He was discharged after three months' treatment with 95 per cent hæmoglobin and 5,000,000 red cells.

At the end of January he began to develop a colour index below unity when he was put on iron and ammonium citrate, 30 grains, thrice daily. The resulting rise in hæmoglobin and red cell counts as the result of iron treatment is well shown in the chart.

The patient has been readmitted into the Mayo Hospital on 2nd July, 1939, with the same complaints. His present laboratory reports are—Hæmoglobin 25 per cent (Sahli), total red cells 1,430,000, total leucocytes 3,125, polymorphonuclears 62 per cent, lymphocytes 36 per cent and eosinophils 2 per cent.

The film shows marked poikilocytosis and anisocytosis. No nucleated red cells are seen. Size by Eve's halometer—8.2 to 8.6 micra, colour index 1.08, reticulocytes 3 per cent.

The van den Bergh reaction—delayed direct and indirect reactions positive. Icteric index—4.

**Gastric analysis.**—No free hydrochloric acid after either porridge meal or histamin.



Sternal puncture

(a) White cell series

Polymorphonuclears	..	38.4	per cent.
Metamyelocytes	..	11.6	" "
Myelocytes	..	20.8	" "
Lymphocytes	..	2.8	" "

(b) Red cell series

Normoblasts	..	14.0	per cent.
Erythroblasts	..	3.6	" "
Megaloblasts	..	8.4	" "

Two megaloblasts whose cytoplasm was polychromatophilic were also seen.

Mean corpuscular volume—112.

Ratio of (a) to (b)—2.5 to 1.

This case is still in the hospital and under treatment with Lilly's concentrated liver extract.

The curious feature of the case is the absence of nucleated red cells from the peripheral blood, otherwise he is a typical pernicious anæmia case, with the typical response to purified liver (anahæmin). The relapse in the blood picture is due to his stopping treatment when leaving hospital.

Case 2.—Hindu, male, aged 22.

Complaints.—Diarrhœa for six months, weakness and low irregular fever.

Condition on admission.—Wasted, severe anæmia and some dehydration of tissues; stools 20 daily, fluid, no mucus, or blood. No evidence of dysentery or tuberculous infection.

On examination.—Heart not enlarged, but a typical hæmic systolic murmur heard. Spleen and liver not palpable; tongue normal; teeth and gums normal. Central nervous system, nothing abnormal found.

Blood examination.—Red cells 1,500,000 per c.mm.; hæmoglobin 40 per cent; colour index 4/3; leucocytes 11,500 per c.mm.; size of red cell, 8.6 micra; anisocytosis, marked poikilocytosis, and megaloblasts present.

Gastric analysis.—No free hydrochloric acid after porridge meal, or after histamin injection.

Stool examination.—No amœbæ, cysts or ova.

Urine.—No urobilin, albumin in traces.

van den Bergh.—Indirect reaction positive.

Treatment.—For three weeks before diagnosis was made, iron and ammonium citrate was given, 30 grains thrice daily, and condition became worse.

Pernamon forte (Organon Laboratories) 5 c.cm. intramuscularly for two consecutive days were given. The blood count improved for two weeks and then remained stationary. There was a typical reticulocytic response, 60 per cent after one week. As the effects of Pernamon appeared to last for two weeks only, a weekly injection of 5 c.cm. was given until the red cells reached 4,750,000 and hæmoglobin 90 per cent.

From this it appears that Pernamon should be given at weekly or fortnightly intervals and not at intervals of one month as the makers recommend.

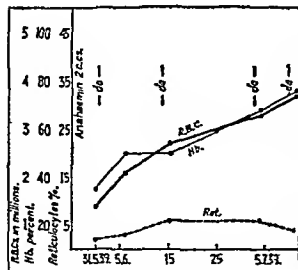
The clinical picture improved as soon as the liver treatment began and the diarrhœa stopped, almost immediately. This case appears to be a typical one.

Case 3.—Mohammedan, male, aged 65, a fruit-seller by profession.

Admitted on 8th June, 1939.

Complaint.—Difficulty in swallowing and sensation of food sticking at the upper part of the œsophagus and severe muscular weakness for three months; low irregular temperature for 20 days; tingling sensations and anæsthesia of hands.

Symptoms increased gradually and he often fainted on standing. No history of diarrhœa.



Case 3.

Examination.—Lemon colour of the skin; heart normal; the muscles were flabby; spleen not palpable; liver palpable; reflexes normal.

Blood examination.—

Date	Total red cells in 10 <sup>6</sup> per c.mm.	Hæmoglobin, per cent	Size of red cells, $\mu$	Reticulo-cyte count, per cent
31-5-39	1.40	35	8.1	2
6-6-39	2.10	50	8.1	3
15-6-39	2.75	50	7.8	6
4-7-39	3.75	68	7.9	6
11-7-39	3.75	75	7.7	4

The leucocyte count was 8,000 per c.mm. on 31st May.

In the film, poikilocytosis and anisocytosis were present, but no nucleated red cells.

Stools.—Negative. (No worms passed after a dose of carbon tetrachloride and oil of chenopodium.)

Gastric analysis.—No free acid after porridge meal, or histamin injection.

van den Bergh.—Indirect weak positive; icteric index 6; sedimentation rate (Westergren) 6 mm. in one hour.

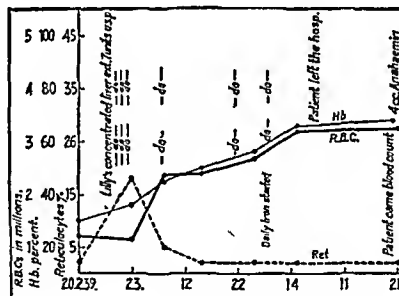
Wassermann reaction.—Negative.

He was given anahæmin intramuscularly and the response in red cells and hæmoglobin is shown in the figure.

No rise in the reticulocyte count was found.

He was examined under a screen, but no abnormality of the barium on its way down the œsophagus was noted. The complaint of dysphagia and anæsthesia has disappeared though the tingling sensation is still present. The patient is still in the ward at the time of writing.

Case 4.—Sikh, male, aged 40, admitted on 20th February, 1939.



Case 4.

Complaints.—Breathlessness and exhaustion on exertion; soreness of buccal cavity; diarrhœa (four stools a day), for last 15 months. All the complaints had been progressively increasing.

On admission.—The patient was anæmic and lean-built; his skin was a greenish-yellow hue.

Examination.—Slight œdema of the feet and ankles; ulceration of the mucous membrane of the cheek; no other physical sign.

Blood examination.—

Date	Total red cells in 10 <sup>6</sup> per c.mm.	Hæmoglobin, per cent	Size of red cells, $\mu$	Reticulo-cyte count, per cent
20-2-39	1.20	30	8.4	2
2-3-39	1.20	35	8.4	18
8-3-39	2.40	45	7.8	5
15-3-39	2.40	50	7.9	2
25-3-39	2.70	55	7.6	2
2-4-39	3.30	66	7.8	2
21-4-39	3.30	66	7.6	2

The leucocyte count was 6,250 per c.mm. on 20th February.

*van den Bergh test.*—Indirect positive.

*Sternal puncture.*—Megaloblastic reaction.

*Gastric analysis.*—No free acid present after porridge meal or histamin injection.

*Urine.*—Normal.

*Treatment.*—He was put on Lilly's concentrated liver extract, 7 U.S.P. units on 26th February. The treatment and response is well shown in the figure.

The peak of reticulocytosis reached 18 per cent only, after six days. He was put on iron and ammonium citrate on 26th March.

When the hæmoglobin had reached 60 per cent, he left the hospital and has been coming for anahæmin injections and blood counts every 15th day.

When he was discharged from the hospital, the gastric test meal was repeated and no free acid was found. The van den Bergh test was repeated and found to be negative.

*Case 5.*—Hindu, female, aged 25, admitted on 10th April, 1939.

*Complaints.*—Progressive weakness in her lower limbs for the last nine months with subsequent inability to walk for the last two months. Started as numbness of the fingers and toes, being transitory in the fingers but spreading in the legs.

Anorexia and discomfort after meals for 15 days.

*Previous history.*—Diarrhœa four years ago for seven months commencing after child-birth—relieved by an injection of campolon. Similar attack about ten months ago, for ten days.

She had been on irregular treatment with campolon, for the last four years. No further pregnancies had occurred.

*On examination.*—She had a lemon yellow colour and was quite plump. Weakness of the lower limbs with slight spasticity; tendon reflexes exaggerated; Babinski's sign was positive and the abdominal reflexes lost; ankle clonus present.

Numbness and icy coldness were complained of. Sensations were intact; sense of position in the toes and sense of vibration in the tibia were much impaired.

No tenderness of the calf muscles. No trophic changes present.

Tongue, raw and red.

*Blood examination.*—Hæmoglobin 75 per cent; red cells 3,170,000 per c.mm.; colour index 1.2, size 7.6 micra; leucocytes 8,126; polymorphonuclears 64 per cent; lymphocytes 26 per cent; monocytes 2 per cent and eosinophils 8 per cent.

Anisocytosis and poikilocytosis present. A few nucleated red cells on 15th April, 1939. Hæmoglobin 75 per cent; red cells 3,300,000 per c.mm.; size 7.6 $\mu$ ; leucocytes 7,500 per c.mm.

*van den Bergh.*—Indirect faintly positive.

*Spleen.*—Palpable.

*Gastric analysis.*—No free hydrochloric acid after porridge meal or histamin injection.

*Stools.*—A few hookworm ova present.

*Urine.*—Albumin and urobilin in traces.

*Sternal puncture.*—Megaloblastic reaction.

The patient was given Lilly's concentrated liver extract and the reticulocyte response, 15 per cent, was obtained after six days.

The blood picture improved, but there was no improvement in nervous signs.

At the time of discharge blood picture was hæmoglobin 85 per cent; red cells 4,150,000 per c.mm.; colour index, 85/83; size of red cells 7.41 micra.

This is a typical case with sub-acute combined degeneration of the cord. Three other cases of sub-acute combined degeneration have been in the hospital during the last year but did not show typical pernicious anæmia blood picture.

#### POST-MORTEM REPORT NO. 1

Hindu, female, admitted on 14th March, 1939. At the time of admission, the patient was comatose. The history available was that she was given some medicine

by a quack which caused diarrhœa for the last three days.

No diagnosis could be reached.

Blood picture was hæmoglobin 20 per cent; red cells 680,000 per c.mm.; colour index 1.4; size 8.6 micra; leucocytes 8,000 per c.mm.; polymorphonuclears 38 per cent; lymphocytes 62 per cent.

Many normoblasts, rare megaloblasts, anisocytosis and poikilocytosis.

Before blood transfusion could be arranged, the patient died two hours after admission.

*Post-mortem report.*—A middle-aged anæmic subject with slight œdema of the feet.

*Respiratory system.*—No abnormality except hypostatic congestion of the lungs.

*Circulatory system.*—The heart showed excessive deposit of fat in the epicardium especially lining the papillary muscles.

Left ventricle showed patchy red and pale 'tabby cat' appearance, valves healthy.

*Abdomen.*—The stomach showed atrophic areas and contained 12 ounces of dark-coloured fluid with no special smell. No other abnormality.

*Spleen.*—Normal in size, hard and fibrous—slate grey in colour.

*Liver.*—Pale yellow in colour; gave Prussian-blue reaction.

*Kidneys and suprarenals.*—Both kidneys pale in colour. Excessive deposits of fat in the pelvis. Prussian blue reaction—negative.

No abnormality in bladder and pancreas.

*Bone marrow.*—It was a deep red colour throughout. Prussian-blue reaction not well marked.

*Nervous system.*—Not examined.

*Sections.*—

Liver showed fatty degeneration with golden-brown pigment in liver cells.

Spleen showed dilatation of venous sinuses and hyperplasia of the malpighian corpuscles.

Kidneys showed hyperactivity of glomeruli, here and there, otherwise no abnormality.

*Stomach.*—Only muscular coat present; no mucous coat.

*Bone marrow.*—A few megaloblasts and normoblasts present.

*Diagnosis.*—Pernicious anæmia.

#### POST-MORTEM REPORT NO. 2

Sikh, male, aged 40; admitted on 10th February, 1938.

*Complaints.*—Severe anemia and abdominal pain of 2½ months' duration. The patient died before complete clinical and laboratory examinations were done.

*Post-mortem report.*—Body well developed, with marked pallor.

*Respiratory system.*—Pleural adhesions on both sides; the lungs were healthy and showed no evidence of disease.

*Heart.*—Hypertrophied, left more than right.

Right auricle was full of blood and the whole right side dilated. Endocardium showed 'tabby cat' striations.

*Abdomen.*—Localized peritonitis over the dome of right side of liver; stomach showed minute hæmorrhages, and no other pathological appearances.

*Spleen.*—Marked splenitis.

*Liver.*—Lemon yellow colour and showed Prussian-blue reaction.

*Kidneys.*—Marked pallor and fine cysts on the surface of both the kidneys.

*Bladder and pancreas.*—Normal.

*Bone marrow.*—Deep red and gelatinous.

*Nervous system.*—Nil.

*Sections.*—

*Heart.*—Fatty degeneration.

*Spleen.*—Trabeculae increased and passive congestion.

*Kidneys.*—Passive congestion.

*Bone marrow.*—Megaloblastic reaction.

*Liver.*—Deposits of hæmosiderin and patchy necrosis.

(Continued at foot of next page)



## M 3, A NEW DRUG IN THE TREATMENT OF MALARIA

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THE Italian Biochemical Institute of Milan which have introduced the antimalarial drug to which the trade name of 'M 3' has been given, claims that this preparation not only confers absolute protection against malaria on an individual which may last for about 6 months in the tropics, but that it is also capable of preventing relapses. It is also claimed as a curative in chronic malaria, and it is said that the cure is brought about by the destruction of the gametocytes. A marked diminution in the size of the spleen and improvement of the general condition of the patients are said to follow its administration in such cases. The manufacturers recommend treatment of acute cases with quinine, after which they advise that M 3 should be prescribed.

The fact that this preparation does not possess any prophylactic properties has already been pointed out by Chopra and Basu (1939). In the experimental work which these authors carried out, volunteers who had been given the prescribed course of M 3 were allowed to be bitten by *Anopheles stephensi*, artificially infected in the laboratory. The infection developed in due course.

Our conception of the part played by gametocytes in causing relapse is quite clear and therefore if the drug has any action in preventing relapse it can only do so by destruction of the asexual forms of the parasites.

(Continued from previous page)

### Acknowledgments

We wish to thank Lieut.-Colonel Amir Chand, I.M.S., Professor of Medicine, King Edward Medical College, Lahore, for allowing us to publish his cases, Dr. Pran Nath Chhuttani, M.B., B.S., for doing the blood counts of the recent case and Dr. Vishwa Nath, Assistant to the Professor of Pathology, K. E. Medical College, Lahore, for the post-mortem reports.

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The manufacturers, at the time they sent this drug to us, assured us that it had stood and would stand any clinical tests. This induced us to assess its value in the treatment of malaria, and investigations were carried out on the following lines in the Carmichael Hospital for Tropical Diseases :—

(1) The action of M 3 on the sexual and asexual stages of plasmodial parasites of man was determined.

(2) Its power of preventing relapse was observed.

(3) Its utility in the treatment of chronic malaria was estimated.

The type of cases experimented upon and the results obtained are recorded below :—

*Case 1.*—A student, who was admitted into the Carmichael Hospital for Tropical Diseases, and showed malignant tertian rings and crescents in his blood, was put on a course of M 3, one tablet daily. His fever was not checked in the course of four days. On the other hand, it increased to such an extent that he had to be treated immediately with quinine and plasmochin. Just before quinine was administered, laboratory-bred *A. stephensi* were fed on him. The occurrence of infection in the salivary glands in due course clearly indicated that the crescents had not been acted upon by this drug. The patient was thereafter put on a full course of M 3 and, as he was discharged before the course was completed, the matron of the hostel where he was staying was specially instructed to see that the rest of the course was given to him in the morning in her presence. After an interval of a month, he was given another course of M 3, and we are satisfied that the patient took this medicine regularly, according to our instructions.

Soon after the termination of the second course, he had two attacks of fever and each attack was temporarily checked with quinine. As he showed no signs of improvement, and as the spleen was considerably enlarged, he had to be treated with ordinary antimalarial remedies.

*Case 2.*—The patient was admitted with malaria and malignant tertian rings in fair numbers were detected in blood smears. He was put on M 3, one tablet a day, which was discontinued on the fourth day on account of a high rise of temperature which necessitated treatment with quinine. He was again put on a course of M 3 and the directions given by the makers were strictly followed. Towards the later stage of its administration, he had a relapse which was treated with quinine; M 3, however, was not discontinued. Soon after the fever was stopped gametocytes made their appearance in the peripheral blood and continued to be present in spite of the fact that M 3 was being administered. They were later destroyed by treatment with plasmochin.

*Cases 3, 4 and 5.*—Three volunteers, who had been given a regular course of M 3 as prescribed by the manufacturers, were successfully infected with malignant tertian malaria by the bites of *A. stephensi* one month after this drug was stopped. The fever induced by the mosquito bites was treated with M 3, and when it was found that the drug made no impression in regard to fever and parasites in the peripheral blood it became necessary to treat them with quinine. One of these patients had four relapses and the other six in course of three months. During the period they were under M 3, crescents appeared in the blood of two of them. *A. stephensi* fed on one of them, even after a fortnight of M 3 treatment, became infected.

*Case 6.*—This patient had suffered from chronic malaria for a long time. Blood examination at the time of his admission showed rings and gametocytes of *Plasmodium malariae*, though there was no fever and the spleen was considerably enlarged. He was put on a course of M 3, but treatment for ten days had no

## ACTION OF ATEBRIN ON MENTAL PATIENTS—A CLINICAL STUDY

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DURING the severe malaria epidemic in Ceylon during 1935–1936, psychotic symptoms were observed in a few malarial patients concurrent with the administration of atebtrin. Drs. Fernando and Wijerama (1935) reported a case. A similar case treated successfully at the Mysore Government Mental Hospital, Bangalore, was reported by me (Govindaswamy, 1936). As atebtrin is an extensively used synthetic antimalarial, it is important to know whether (i) it is atebtrin that is directly responsible for the mental and neurological symptoms reported in these cases, or (ii) whether atebtrin merely precipitates a pre-existing disposition to mental disorder. A third possibility would be that in these cases it is the malaria, whose cerebral symptoms are well known, that is responsible for observations of this kind, whilst atebtrin on account of some defective metabolism is rendered inert.

Similar work not having been done elsewhere, it was thought that there might be a partial solution to some of these questions, if patients who showed definite derangement in their psychological personality were put under the action of atebtrin, and observations made whether this drug produced any specific reactions in such cases.

As a first step in such work, twelve schizophrenics, six manic-depressives, and six deliriod patients were put under the action of atebtrin, and the effects studied. The atebtrin, which was supplied free by Bayer Remedies Limited, was administered as hypodermic injections, which were given daily in doses of 0.1 gramme, the injections being stopped only when the patients showed some unequivocal symptoms.

These experiments were started in May 1936. Since their continuation depended on suitable cases being available, they were concluded for purposes of the present paper only in May 1938. The observations reported refer to groups corresponding to well known

reaction types—schizophrenic, manic-depressive, and deliriod. In only three cases was it found necessary to report in some detail observations on individual patients. The group observations suffer from one limitation, common in psychiatry, namely, that the diagnostic labels are merely descriptive terms. But every precaution was taken to ensure that the patients in the same group had a large common measure of signs and symptoms. All patients were in-patients of the Mysore Government Mental Hospital, Bangalore, except one who was seen in consultation outside.

*Schizophrenic group.*—As it was not known how large quantities of atebtrin might affect mental patients, only confirmed schizophrenics, with signs and symptoms of about two years' duration, were selected in preference to more useful members of the community. Twelve male patients between the ages of eighteen and thirty and who were in good physical health were chosen. Their education averaged from primary to high school standard, and their economic condition was marginal. The reaction type was catatonic. Disconnections, meaningless excitement, negativism, and stupor were exhibited some time or other, in various degrees, by these patients. All of them had suffered from malaria previously, but none immediately prior to or during the experimental work.

Every one of these patients withstood large quantities of atebtrin before showing toxic symptoms. The minimum amount administered before such symptoms were observed was fifteen daily injections of 0.1 g., and the maximum twenty-five. In one patient, forty-two injections were necessary before any toxic symptoms were noticed.

*Physical symptoms.*—(1) The earliest toxic symptom noted was a chalk-like pallor of the face, gradually changing to yellow. The skin of the whole body next took on this colour, and the eyes were affected last. In only half of the patients did the eyes turn yellow, in the other half the colour was a dirty blue. While the yellow colour could be accounted for as being due to the deposit of atebtrin, the blue colour cannot be explained so easily. In only one patient, jaundice supervened in addition, as shown by rigors, pain in the hepatic area, clay-coloured stools, intense itching and increased coagulation time of blood to nearly four minutes.

(2) Gastro-intestinal symptoms, such as anorexia, vomiting, and in two patients diarrhoea, were observed after the fifth injection. The chief neurological symptoms observed were nystagmoid jerks, giddiness, partly due to the nystagmus, coarse tremors of the hands, ataxia, which was worse when the eyes were closed, and multiple neuritis. This neuritis, associated with decreased tone of the muscles, involved both the extensors and the flexors of the forearm, hand, calf, and foot

(Continued from previous page)

any reagent to inhibit or destroy the contaminating organisms. Satisfactory results are obtained when fresh specimens of sputum collected in ordinary clean sealed jars are used for the intradermal test.

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muscles with corresponding defects in grasping, standing, and walking. Actual wasting of the peroneal muscles was noticed in two cases. All patients recovered from their neuritis with rest, cessation of the drug, feeding with vegetable salads, fruit juices and injections of concentrated vitamins B and C, parenteral liver extract, and intravenous administration of sodium thiosulphate (30 grains for three days).

(3) The temperature rose in eight patients, to a maximum of 102 degrees to 103 degrees and was maintained at that level from a minimum of ten hours to a maximum of six days. Whether this rise in temperature is a toxic symptom of atebtrin, or due to an unrecognized infection, it is difficult to say. The temperature came down in all cases with rest, cessation of the drug, and with the administration of omnadin and cytotropine.

(4) Leukopenia was noted after the tenth injection, the fall in the polymorphonuclears being more than in the lymphocytes. No detailed examinations were made and the ordinary examination of blood films did not show any abnormal cells.

(5) A fall in blood pressure was noted in every case, within half an hour after injection, but the fall was not so severe as to cause alarming symptoms.

(6) Routine examination of the urine did not show any abnormality, except that atebtrin could be detected in it for weeks afterwards.

(7) All the patients did not show all the symptoms, because the injections were discontinued as soon as a toxic symptom of any severity was noticed.

*Mental symptoms.*—Mental changes were observed in the case of every patient, which were qualitatively similar, but quantitatively different.

(i) The general tendency was towards reduction of catatonic and negativistic symptoms. The patient became more friendly and co-operative and the stuporous patients had better contact with their environment. This improvement was only temporary, the patients relapsing into their original condition in a few hours to a few days.

(ii) Intellectual disconnections and feelings of unreality, characteristic of these patients, but masked by their morbid introversion; was brought more to the surface during atebtrin administration.

It must be remarked, however, that these effects are not specific to atebtrin. The majority of schizophrenic patients show good contact with their environment, under the influence of any drug, or disease, which violently alters their somatic status.

*The manic-depressive group.*—Six patients, between the ages of 22 and 38, of average physical health, were studied in this group. Three of them were depressed, and three were hypo-maniacal. The criteria of diagnosis were

(i) a previous attack, (ii) absence of disconnections, (iii) a pyknic build, and (iv) the presence of an hereditary factor.

None of the patients in this group could stand such large doses of atebtrin as the schizophrenics. Every patient began to show toxic symptoms with the fifth injection and they were immediately discontinued. Fall in blood pressure, alteration in the colour of the skin, slight ataxia, were amongst the earliest symptoms noticed. The subjective experiences of these patients are interesting. (i) All the patients complained of paræsthesia in the tips of their fingers and toes, numbness of the face and funny feelings regarding their body, a feeling that their limbs had changed their shape and size. (ii) Auditory and visual perceptions were intensified in the early stages, the patients saying that they could hear and see more clearly. This intensification was common to both the depressed and elated patients, and hence it is not probably due to the lowered threshold of sensibility commonly observed in maniacal patients. Alteration in time perception was in the direction of lengthening.

(iii) During the period of atebtrin administration, no perceptible change was noticed in the maniacal patients, but the depressives were definitely less miserable.

The following case report of a cyclothyme patient seen in consultation is interesting:—

The patient was a sturdy Englishman, about 40 years of age, of a pyknic build, well placed in life, who, suffering from malaria, had two injections of atebtrin (0.1 g.), the second injection two days after the first. No untoward symptoms were noticed after the first, but two hours after the second injection, he felt giddy, and faint. He was brought to in a few minutes, with smelling salts, a coramine injection and hot coffee. When seen within an hour after this attack, he complained of disturbances in perception, almost exactly similar to those described above. Being well educated, and intelligent, he gave a clear, reliable account. He said that he felt as if the whole of the right side of the body did not belong to him and that he was floating in space. He had a feeling that a very big, oversized, but very light half of the body was loosely joined to his left half. It appeared to him that all the furniture in the room had become disarranged, and solid old-fashioned heavy chairs and tables looked angular and modernistic. No definite neurological changes could be made out, but it seemed that space localization, and stereognosis were rather defective. His blood pressure was 140-95, his arteries did not show any atheromatous changes, the fundus was normal, and his blood Wassermann reaction negative. The patient recovered completely in a few hours.

A significant point in the history of this patient was that he was a confirmed alcoholic with an euphoric personality, but with no history of any alcoholic neuritis or delirium tremens. The experience of my medical colleagues and myself has been that alcoholics do not stand atebtrin well.

*Delirioid patients.*—Atebrin was administered to six delirioid patients, the object of study being only to note whether the confusion and restlessness was intensified or not. These

delirious patients were suffering from different diseases, pyrexias of unknown origin, puerperal sepsis, syphilitic excitement and anæmias, the only common symptom being confusion and disorientation. Not more than five injections were given, and the tendency in all cases was towards decrease and definitely not an increase in the deliriod state. Delirium and epileptiform attacks have been included in the reports of toxic symptoms of atebtrin (Findlay), but they were not observed in our patients.

The following case report of a patient is of interest in this connection :—

A Mohammedan woman, about 40, lean, weak, and anæmic, was transferred from St. Martha's Hospital, to the Mental Hospital, Bangalore. The history was that she was admitted to the hospital suffering from malaria (benign tertian parasites found in the blood), and was being treated only with quinine. Two days prior to transfer, she became restless, confused, difficult to control, and developed auditory and visual hallucinations. These abnormalities were present in the apyrexial period when she was examined at the Mental Hospital, but were more intense when she had fever.

She was given four daily injections of atebtrin (0.1 g.). As she was also slightly jaundiced and weak on admission she was given cytotropine and coramine, as injections, and liver extract and iron by the mouth. After a week, not only was she free from fever, but became more co-operative and rational. Atebtrin was stopped and she was given a stimulant, and anti-anæmic line of treatment. She was discharged from the hospital, recovered, in a month.

An unexpected opportunity was afforded for further study of the case reported by me in the *Lancet*, a year after his discharge, when he interviewed me as a follow-up case. He was a thick-set man who looked fit and healthy, and for experiment he was given one injection of atebtrin (0.1 g.). In a few minutes, he began to talk incoherently, became confused, and disorientated, and he showed coarse nystagmoid jerks. He recovered completely in two hours with rest and a cup of hot milk. It would be of great interest if other doctors, who have reported cases of atebtrin psychosis, could administer small doses of atebtrin to those patients in their normal phase and see whether they develop any abnormal mental symptoms.

### Conclusions

Our study has been incomplete in many respects, and the conclusions are mostly negative. The following conclusions however seem to be of some positive significance :—

(i) Atebtrin in medical doses is well tolerated, and the toxic dose is high.

(ii) The physical signs and symptoms of toxicity are gastro-intestinal disturbances, rise in temperature, fall in blood pressure, leukopenia, and multiple neuritis.

There have been very few reports of serious damage to the liver, kidneys, or blood cells, although they play a very important part in the absorption and excretion of synthetic anti-malarials. It is obvious that in severe

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## A SIMPLE ANÆSTHETIC APPARATUS

By E. M. SEWELL

MAJOR, I.M.S.

Bellary

IN the apparatus about to be described I make no claim to originality in design. It has been my endeavour to find the simplest form of anæsthetic apparatus which could, with slight adaptation, be used with reliability for intra-tracheal, intra-pharyngeal, or intra-nasal induction using ether with air or oxygen. This apparatus has been in constant use for the past 3½ years in certain Indian military and civil hospitals by comparatively inexperienced anæsthetists who quickly learned its use, and in whose hands no mishap occurred, a satisfactory standard of anæsthesia being obtained with few exceptions. The apparatus was made for me by Messrs. Charles A. King Ltd., 34, Devonshire Street, London, W. 1.

The apparatus consists of :—

- (1) A Kilner jam or fruit preserve jar of 2 pounds capacity (see figure, 6).
- (2) A Boyle's sight feed tube incorporated in the Kilner jar cap (7).

The following accessory items are also necessary :—

- (1) Magill spatula (laryngoscope) (2).
- (2) Magill introducing forceps (1).

(Continued from previous column)

hepatitis, nephritis, and anæmia, atebtrin should be cautiously administered.

(iii) Since nystagmus and ataxia were exhibited by the majority of our patients, these symptoms were most likely due to atebtrin. Inflammatory gliomatous reactions and necrosis in the corpus callosum and cerebellum due to parasitic emboli, which have been described in malaria (Duerek), did not occur in our cases.

(iv) The mental symptoms are confusion, disorientation, emotional instability, and severe insomnia. They are due to atebtrin, but occur only in a minority of patients who have an idiosyncrasy to the drug.

(v) Manic-depressives, cyclothymes, alcoholics, arterio-sclerotics, and people of a pyknic build, do not tolerate atebtrin in large doses. Since these conditions are usually inter-related, idiosyncrasy to atebtrin can well be looked for in this group.

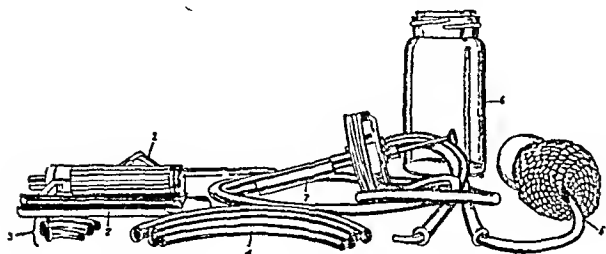
### Summary

Atebtrin in large doses was administered to groups of mental patients suffering from well recognized psychiatric syndromes and the results of such administration are reported.

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- (3) Magill india-rubber intra-tracheal curved catheters (4).
- (4) Magill metal connections (assorted sizes) (3).
- (5) Hand bellows (6).
- (6) Spare dry cells and lamps for (1).



After continuous use I can make the following claims for it :—

- (a) Extreme simplicity in construction, maintenance and use.
- (b) Reliability.
- (c) Low initial cost and upkeep, with ease of replacements.
- (d) Portability.

(a) The system used is extremely simple and a variable concentration of ether is obtainable by means of the Boyle's adjustable tube. The apparatus is easily cleaned. Sub-assistant surgeons have quickly learned to give intra-nasal and intra-pharyngeal anæsthesia and to maintain intra-tracheal after the introduction of the catheter. For dissection of tonsils the apparatus is connected to the anæsthetic tube of the tongue depressor of the Boyle-Davis or other gag used. By connecting the apparatus to a glass or metal spiral coil in a thermos flask, warmed ether may be given when necessary. Air is blown through or over ether, either by means of hand bellows or a motor-driven blower. If desired an oxygen cylinder may be connected to the air inlet of the jar.

(c) The cost of the jar and Boyle's tube is £1 17s. 6d.

The cost of accessories is approximately £6 10s.

The cap of the Kilner jar has the great advantage that it is standard in diameter for all capacities of jar made. The jar itself is procurable from many European or Indian grocery firms, and, if broken, can thus be replaced with the minimum of delay. I have not included among the accessory items any form of airway. I maintain that no anæsthetized patient should ever be permitted to leave the operation table without the introduction of an airway, yet I have often been struck, not only by the neglect in many Indian hospitals to observe this golden rule, but by the complete absence of any form of airway.

I have found the above form of anæsthetic apparatus so eminently useful in practice that I venture to hope that others, should they decide to adopt it, may find it equally so.

## VITEX PEDUNCULARIS IN THE TREATMENT OF BLACKWATER FEVER

By J. E. MEASHAM, M.D.

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THE writer's attention was drawn to *Vitex peduncularis* by Messrs. James Finlay & Co., Ltd., Calcutta, in March 1936 by means of an extract from Circular No. 1 (1936) of the Doonars Planters' Association. The extract was entitled 'Vitex Peduncularis and Blackwater Fever' by L. J. de la Nougerede.

In April 1936 Dr. D. Finlayson of Munnar, Travancore, kindly sent me a report from Mr. C. Rowson, a planter of great experience from the same district. Mr. Rowson wrote :—

'I find that *Vitex peduncularis* does not grow in South India or Ceylon, but many kinds of the same family (*Verbenaceæ*) do grow in both places.

*The Forest Trees of Travancore* by T. F. Bourdillon, F.L.S., late Conservator of Forests, Travancore, mentions under Order *Verbenaceæ* :—

- (1) *Vitex altissima*. (2) *Vitex negundo*. (3) *Vitex pubescens*. (4) *Vitex leucorhylon*.

Under *Vitex negundo* he writes—"the leaves, root-bark and flowers are employed in local native medicine, the leaves as a tonic and vermifuge, the flowers as an astringent, the root-bark as a tonic". The Indian list of medicinal properties of the plant is however much larger than the Ceylonese and includes headache cures, and cures for rheumatism and bladder complications. I am therefore of the opinion that, if four of this family grow in South India, the other member—*peduncularis*—will also grow.

In view of Mr. Rowson's opinion the writer asked Messrs. James Finlay & Co., Ltd., for a supply of seeds and these were received in July 1936. Out of one hundred seeds, four were germinated. One of these plants died, but three remain and have after nearly three years attained a height of over five feet.

*References in the literature.*—J. C. S. Vaughan (1921) described his experience with *Vitex peduncularis*. He claimed good results in eight cases of malaria and recovery in three out of four cases of blackwater fever thus treated.

Chopra, Knowles and Gupta (1924) used this drug in a series of cases of malaria and concluded their paper as follows :—

(1) 'Chemical analysis of the dried leaves of *Vitex peduncularis* shows the presence of traces of an alkaloid.

(2) In our series of cases of malaria fever, however, caused by *P. vivax*, *P. malariae* and *L. malariae*, the freshly prepared infusion of dried leaves had no effect whatever on the

parasites in the blood, on the temperature chart, or on the other clinical symptoms.

(3) The drug appears to be absolutely useless in the treatment of malaria.'

Their conclusions are directly opposite to those of Colonel Vaughan in so far as malaria is concerned, but they did not try the drug in blackwater fever.

#### *The present series*

This consists of eleven cases which have occurred in the Anamallai Hills from 1936 to 1939. The area is situated in the South-Western Ghats and is approximately seventy square miles in size. The centre of the district is the township of Valparai, 3,700 feet, latitude

10° 20' N. and longitude 76° 57' E. The malaria transmission season is from February until the break of the south-west monsoon in late May or early June. The transmitting agent is *A. fluviatilis* (Measham and Chowdhury, 1934); no other species out of a total of nearly 10,000 mosquitoes dissected to date by the laboratory technicians of the local centre of the Ross Institute, working under the writer's direction, having been found infected.

Blackwater fever is a rare condition in the district, four cases occurring on the average annually in a practice which cares for some 13,000 persons.

The main features of the eleven cases are now given in tabular form.

*Table showing the results of treatment of blackwater fever with infusion of Vitex peduncularis*

Case number	Race	Sex	Age	Type	Malarial parasites	Spleen, fingers below costal margin	Additional treatment	COURSE AND DURATION		Result
								Days in hospital	Day urine cleared	
1	Malayalee	M.	40	Severe. T. 103° on admission. Continuous vomiting.	Nil	1	..	7	3	Cured.
2	Malayalee	F.	1½	Severe. T. 105°. Severe vomiting. Profound anæmia.	M. T. rings	8	Atebrin 2 doses.	12	3	Died.
3	Tamil	M.	22	Severe. T. 103°. Vomits everything.	Nil	Nil	..	15	3	Cured.
4	Malayalee	M.	35	Admitted for clinical malaria. Blackwater on 2nd day. Moderately severe.	Nil	Nil	Quinine for 1 day.	11	2	Do.
5	Malayalee	M.	24	Severe. T. 103°. Vomiting.	Nil	Nil	One dose of atebrin.	29	3	Do.
6	Malayalee	M.	25	Moderately severe. T. 101°. Vomiting.	Nil	2	One dose of atebrin.	10	3	Do.
7	Tamil	F.	38	Very severe. Intense vomiting. T. 103°.	Nil (pigment)	4	Strychnine and digitalin as required.	24	4	Do.
8	Malayalee	M.	19	Severe. T. 104°. Vomiting.	Nil (pigment)	5	..	22	3	Do.
9	Malayalee	M.	27	Severe. T. 104°. Vomiting.	B. T. rings	Nil	Quinine for 1 day.	21	4	Do.
10	European	M.	25	Admitted for malaria. Blackwater on 3rd day.	M. T. rings	Palp.	A course of atebrin.	19	2	Do.
11	Tamil	F.	33	Severe. T. 104°. Vomiting.	Nil (pigment)	4	..	21	4	Do.

*Note.*—Eight cases occurred in the malaria transmission season. There was hæmoglobinuria and albuminuria in every case; in case 9 there was suppression for one day.



A study of the above table brings out the following points:—

*Race*.—The series comprises seven Malayalees, three Tamilians and one European. Malayalees do not comprise more than 5 per cent of the population, and this incidence appears to show a racial susceptibility.

*Sex*.—There were eight males and three females in this series.

*Age*.—The average age was 26.5 years, the eldest being 40 years and the youngest 1½.

*Type*.—Except for case 4, all the cases were of a severe type with high fever and intense nausea, vomiting and jaundice. There was suppression of urine in one case for 24 hours.

*Urine*.—There was hæmoglobinuria in each case and the urine was loaded with albumin.

*Blood*.—This was examined on admission to hospital in each case. Three cases showed malarial parasites, two of malignant tertian and one of benign tertian malaria. Three cases showed an increase in the large mononuclear cells which contained hæmoglobin pigment. Five cases showed no evidence of malaria in the blood.

*Spleen*.—Four cases showed no increase in size, three slight enlargement, three moderate enlargement and one gross enlargement.

*Treatment*.—All the cases received an infusion of *Vitex peduncularis*, one ounce being given hourly until the colour of the urine had returned to normal. Thereafter it was continued in the same dose four times daily for a further three days. It is noteworthy that patients who vomited everything else were able to retain the infusion. Five cases had received one or two doses of atabrin or quinine prior to receiving the infusion, but not in sufficient quantity to influence the course of the disease.

Case 10 received a full course of atabrin in addition. All the cases received tonics and liver in some form during convalescence.

*Duration and course of disease*.—The average length of stay in hospital was 17 days, approximately, and the urine was clear on the third day after beginning infusion *Vitex peduncularis*. The general condition improved with the clearing of the urine, though the temperature did not always reach normal until one or two days later.

*Result*.—Only one out of eleven cases died, giving a death rate of 9.1 per cent. Stephens (1937) gives two mortality tables in which the average rates are 20 per cent and 31 per cent, respectively. Manson-Bahr (1935) gives the average mortality as 25 per cent and Rogers and Megaw (1930) as varying from 10 per cent to 40 per cent.

*Conclusion*.—The cases recorded were under the actual care of Drs. Dorai Raj, Mannadiar, Gopalan and Kuppaswamy of the Companies' Medical Department. They and the writer are firmly convinced of the beneficial effects of infusion *Vitex peduncularis* in blackwater

fever, one of its most striking being the rapid disappearance of the severe liver and loin ache which is such a distressing feature of this disease. It has also been noted that the infusion has no effect in albuminuria due to other causes.

### Summary

A series of eleven cases of blackwater fever is given in tabular form and an analysis of the data is made.

It is concluded that the drug is of definite value in blackwater fever and it is hoped that further clinical and pharmacological observations by other workers will be made.

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*Note*.—Chopra (1936), in his *Handbook of Tropical Therapeutics*, summarizes the information on this drug, as follows:—

'*Vitex peduncularis*. This plant grows largely in Bihar, Eastern Bengal and the Central Provinces but it is not very well known. The aboriginal tribes of these localities believe it to have curative properties against malaria, blackwater fever and kala-azar. In Hindi it is known by various names, *Nagbail*, *Nagphani*, *Charaigora*, *Chhagiaruba*, *Minjurgorwa*; in Bengal it is called *Baruna* and *Doda*.

The only reference by the old writers regarding its medicinal properties is its use for external application for pains in the chest. Vaughan (1921) found that the aboriginal tribes of certain parts of Bihar were well acquainted with this plant, and used it in the treatment of malarial fever and also of blackwater fever. They prepare an infusion of the leaves, of the root-bark or young stems and take it internally several times a day with much benefit. Preference is given to the dark-coloured root plant over the pale-coloured variety.

Vaughan (1921) tried this drug in a series of cases in both these diseases and reported that it gave very satisfactory results. Chopra, Knowles and others (1924) carefully tested the drug and found it has no effect whatever in malaria.'

One's suspicion is aroused by the claims (not made by the present writer) that this drug is a specific against malaria and blackwater fever. Even if one does not accept the uncompromisingly condemnatory verdict quoted above, it is obvious that *Vitex peduncularis* is at best a poor anti-malarial drug, and we have good anti-malarial drugs at our disposal.

If it is not on account of its anti-malarial properties, how then does it act? In an attack of blackwater fever there is often one severe hæmolytic crisis in which all the damage is done: in such a case treatment consists in helping the body to tide over the shock, to recover its normal functions and repair the damage. Whilst it is conceivable that there are many drugs that will assist this, there does not seem room here for a 'specific'.

On the other hand, it is conceivable that there might be some specific drug that would prevent further hæmolytic crisis, and would, therefore, if used prophylactically, prevent the initial attack. Is *Vitex peduncularis* such a drug? There is no evidence that it has



Trypaflavine (5 c.cm. of 2 per cent solution) did not produce any improvement either. The temperature persisted with evening rises and morning remissions.

Prontosil album was tried finally: 1.5 grammes were given orally for the first two days. Patient stood the dose well. For the successive seven days 3 grammes were given daily (2 tablets, *t.d.s.*, after food) and finally 1.5 gm. for six days. The temperature dropped to normal after the 4th day of treatment and remained at the normal level. Patients made an uneventful recovery and put on weight. The leucocyte count after prontosil treatment was 6,890 per c.mm.

*Remarks.*—The source of infection in this particular case is puzzling. The patient was with the unit pursuing his normal routine work till the onset of the disease. No other case was reported from the unit. As a Punjabi Mussulman he had no chance of getting into contact with pigs. The probable source of infection was cow's milk, and the patient was possibly susceptible to *Br. abortus*.

Other points of interest were that there were no signs of myocardial involvement throughout the course of the disease, and the pulse remained of fair volume and tension. Urine cultures were sterile for *Br. abortus*.

My thanks are due to Lieut.-Colonel C. H. N. Baker for permitting me to publish the case and to the Lahore District Laboratory for their reports.

## A CASE OF CONGENITAL DIAPHRAGMATIC HERNIA

By B. S. JOSHI, M.B., B.S. (Rangoon)

Civil Assistant Surgeon, Nyaunglebin District, Pegu, Lower Burma

A BURMESE female child, aged 8 years, was admitted into the civil hospital, Nyaunglebin (Burma), on 14th July, 1939, for the treatment of pain in the abdomen and constipation of ten days' duration. The child was very frightened and answered no questions. The parents said that it had had a sudden attack of pain in the abdomen and they had massaged and kneaded the whole abdomen. A Burmese *saisaya* was called in and he administered certain medicines and massaged the abdomen more briskly. After ten days of intensive treatment, the child was brought into the hospital. All along the child had not passed any motion but had vomited off and on. The parents were not sure as to the passage of flatus. The child had been similarly attacked at irregular intervals ever since birth.

On examination, the child was found to be in distress. The breathing was laboured and the abdomen was very much distended. It was tender all over but there was no rigidity. It was tympanitic. No mass was felt anywhere. Liver dullness slightly diminished. On auscultating the abdomen peristalsis was heard. Lungs:—Right lung normal, left lung no breath sounds heard at all, but it was resonant. The child had a temperature of 100°F., pulse 136 and respiration 38 per minute. A provisional diagnosis of intestinal obstruction was made. The parents refused operation. She was given turpentine stupes to the abdomen, placed in Fowler's position, and a turpentine enema was given. The result of the enema was poor. She was given pituitrin  $\frac{1}{2}$  c.cm. and enema repeated in half an hour. The result was again poor, only a little faecal matter coming through. Examination of this motion revealed many ova of roundworms. As I had seen a few cases of mild intestinal obstruction caused by roundworms, I gave her santonin grains 2, calomel grains 2 and sodium bicarbonate grains 5, at night. She passed

a motion next day but brought out no worms. Her temperature was 99°F., the distension of the abdomen was much reduced and she was more comfortable. Her evening temperature was 100.5°F. On the 3rd day her temperature in the evening was 102°F. and she had passed a motion. An enema was given with good result. On the 4th morning she passed four motions by herself in quick succession and her temperature was 101°F. in the evening. On the 5th morning her temperature was 101.5°F. and her abdomen distended again. She was in distress with a fast and feeble pulse. She vomited a large roundworm and died the same evening. Fortunately I was allowed to do a post mortem.

*Post-mortem findings.*—On opening the abdomen, I found the coils of intestine adhering together and thick greenish flakes of pus here and there. A big loop of the transverse and descending colon was seen to go through an opening on the left side of the diaphragm into the left pleural cavity. This could not be pulled out. On opening the chest the right lung was normal but the left pleural cavity was filled with the colon which was found perforated and a bunch of roundworms were coming out of the tear. The left lung was in a very rudimentary condition and had probably never expanded.

### Summary

A fatal case of congenital diaphragmatic hernia is described. The clinical diagnosis was intestinal obstruction probably by roundworms. The post mortem revealed a congenital diaphragmatic hernia with the colon in the left pleural cavity full of roundworms causing obstruction of the large gut. The left lung was found in its foetal condition. The child had had attacks of pain in the abdomen off and on since birth and every time responded to native medicine and massage. The colon was perforated either by the roundworms or the brisk massage and the faecal matter had trickled through the opening in the diaphragm into the abdominal cavity causing peritonitis and death.

### Acknowledgments

My thanks are due to Lieut.-Colonel D. P. McDonald, I.M.S., for his helpful suggestions regarding this case and also to Colonel R. H. Candy, I.M.S., Inspector-General of Civil Hospitals, Burma, for his permission to publish these notes.

## A CASE OF LATE RELAPSE IN TYPHOID FEVER

By V. SIVASANKARAN

CAPTAIN, I.M.S.

Indian Military Hospital, Ferozepore

RELAPSE in 5 to 15 per cent of typhoid fever cases may develop during the actual defervescence but more commonly after an afebrile period of a week or little longer. I am recording the case of a soldier under my care, treated in the medical wards of this hospital, who had a relapse of typhoid, four weeks after the primary attack.

L/D, aged 30, service 12 years in the Indian Army, was admitted to hospital on 27th September, 1938, for fever with rigors, headache and pains all over the body.

*Duration.*—Two days during which period he was detained in hospital.

		T-O	A-O	OXK	OX 19	OX 2
Primary attack.	28-9-38	250	250	175	0	17
	4-10-38	1,250	1,250	85	17	17
	7-10-38	500	500	50	0	0
	17-10-38	700	700	50	0	0
	29-10-38	700	350	35	0	0
Relapse	1-11-38	350	200	50	0	0
	18-11-38	800	400	0	0	0

*Bact. typhosum* isolated from blood.

talking and she could not get sleep. There were also petechiæ and bruises all over the body of various sizes varying from a pin point to 4 inches in diameter.

Temperature 100.8, pulse 124 per minute very poor. Condition was diagnosed as a severe case of scurvy.

The following line of treatment was adopted:—

23-7-1939. Cantan tablets by mouth one every hour. Injection of Cantan 1 c.cm. four-hourly. Also given injection of calcium gluconate 10 c.cm. Previous to admission she had hæmostatic serum.

24-7-39. Injection Cantan forte four-hourly. Injection Redoxon forte 5 c.cm. given intravenously. Cantan and later on Cebion tablets used every two hours. Bleeding was less for about three hours after intravenous Redoxon but again started. Injection antivenin 10 c.cm. also given.

25-7-39. Injection Cantan forte or injection Cebion forte, each containing  $7\frac{1}{2}$  grs. of ascorbic acid was given six-hourly alternating with calcium gluconate and later with injection of Manetol. Bleeding slightly less for about six hours but later again increased and patient started bleeding *per vaginam* also, though her last period was only 15 days ago. Injection antivenin 10 c.cm. repeated.

26-7-39. Injection Cantan forte and Cebion continued six-hourly and two injections of Coagulan (Ciba) given. Tablets continued four times a day.

27-7-39. The same treatment carried on. Improvement definite on the 27th.

28 and 29-7-39. Same treatment, improvement well maintained.

In addition to the above treatment the patient was given calcium lactate 30 grs. and a mixture of iron and arsenic containing 30 grs. of iron and ammonium citrate per dose *t.d.s.* Her mouth was cleaned with hydrogen peroxide every three hours. She was given also alum gargle. Gums were painted with adrenalin 1-1,000. But local treatment did not help at all. Glycerine-ichthyol was applied externally.

Also she was given glucose per rectum, 5 per cent in normal saline, continuously by the drop method for about six days till the bleeding from her gums stopped. At about the same time the vaginal bleeding also stopped.

Wherever she was given an injection she got a 'bruise' and even when given intravenously, there usually was a small hæmorrhage.

Bleeding was slight from the gums after the 31st July when she was given an injection once a day and two tablets three times a day but on the 5th August, 1939, she again started bleeding rather profusely from the gums and a 'bruise' appeared at the site of an injection. Two injections a day for three days stopped bleeding and later once a day up to the 9th August, 1939. Patient still continues to take tablets and will be kept on one tablet first three times, then twice and later once a day.

The temperature continued till the bleeding nearly stopped and bruises disappeared. It again rose with the recurrence of bleeding.

Diet for the first 5 to 6 days was lime squash drinks frequently, and a little milk and ice to be sucked as much as possible. Later on she was given soups, fruit juices, arrowroot, *conjee*, etc., any food which she could take easily.

Patient is still in the hospital; she is doing very well and will be discharged after a few days when she has recovered from her anæmia.

The case is of interest because, although for two or three days there appeared to be no hope of her recovery, persistence in carrying

on treatment with very large doses of vitamin C brought on some improvement after which she progressed very favourably.

[*Note.*—Is the diagnosis of scurvy justifiable in this case?

There are many cases in which some clinical improvement will follow the administration of vitamin C other than frank scurvy. In this case the patient received many other medicaments as well. It seems more probable that it is a case of toxic hæmorrhagic purpura. —EDITOR, I. M. G.]

## A CASE OF TETANUS TREATED WITH 25 PER CENT MAGNESIUM SULPHATE SOLUTION

By J. N. BHATTACHARJEE, L.M.F., L.T.M.

Gopalpur Tea Estate, Dooars, Jalpaiguri

A tea-garden coolie, a female, aged about 65 years, got an injury on the dorsum of her right hand by a paddy-husking machine (*dhenki*). The patient was treated and it healed up completely by the 15th day.

From the morning of the 17th day the patient complained of stiffness of her neck muscles. On the next day she was not able to raise her head from the bed. On the morning of the 19th day I saw her and found the following symptoms:—

Feeling of tightness in the jaws and difficulty in mastication and swallowing.

The angles of mouth drawn out producing *risus sardonicus*.

The patient could not turn herself on her side.

There was no tetanic convulsion of the extremities.

The patient was treated in the following manner:—

She was put in a darkened room, antitetanic serum (1,500 units) was administered once only on the first day of treatment, and she was given a bromide mixture three times a day for ten days.

In addition, 25 per cent magnesium sulphate solution in a dose of 1 c.cm. increased daily by 1 c.cm. up to 5 c.cm. was injected intravenously (total amount 30 c.cm. was administered).

During the course of treatment she showed remarkable improvement and at the end of the second week of treatment she was completely recovered.

Points of interest in the case are:—

There were no general tetanic convulsions.

A relatively small amount of antitetanic serum was administered yet the patient recovered.

Treatment with intravenous injection of 25 per cent magnesium sulphate solution was apparently successful.

The disease began after the primary injury was completely healed.

I am indebted to my chief Dr. T. M. Ghosh for his kind permission to publish this note.

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# Indian Medical Gazette

JANUARY

## PERNICIOUS ANÆMIA IN INDIANS

In these columns some eighteen months ago we discussed the world distribution of disease and its ever-changing picture. Advancing civilization with its facilities for rapid transport has led to the wider distribution of infectious diseases, and with its opportunities for indulgence to the increase in the incidence of metabolic diseases. However, other accompaniments of civilization, sanitary progress and international quarantine regulations, have done much to counteract these ill-effects, have limited the internal spread, and in many cases completely stopped the extension of epidemics from country to country, whilst medical science has devised means of arresting disease in its earliest stages, and thereby limiting its disabling and its infectious potentialities. As well as the actual changes that are occurring there are the apparent changes, changes in our perception of the picture. Classical examples are cancer, which was, not many years ago, considered to be rare amongst the indigenous inhabitants of tropical countries, and enteric which was never diagnosed except amongst Europeans. Time and the advances of medical science have shown that both these conceptions were entirely wrong. The truth is that, as in their physiological make-up there are few fundamental differences between Indians living in the tropics and Europeans living in temperate climates, there are likely to be few absolute differences in the diseases to which they are susceptible, though there are certain to be relative differences in the incidences of these diseases, just as there are between those in different communities in any country.

Pernicious anæmia is a disease which is reported to be rare in Asiatics; frequent references to this observation will be found in the British and American medical literature. On the other hand 'pernicious anæmia', or sometimes more cautiously 'anæmia of the pernicious type', is a common diagnosis in India. The first trouble is the name, which from all points of view is a most unfortunate one, but the name cannot be changed with every advance that is made in our knowledge about a disease; the expedient of attaching the adjective Addisonian, adopted by some writers, has added to the specificity of the name, but has also introduced another element of confusion. Further confusion results from the facts that many physicians refer to all macrocytic anæmias as 'pernicious'; that the majority

of these anæmias respond, to a greater or lesser extent, to injections of liver extract, the specific for 'Addisonian' pernicious anæmia, seems to add justification to this laxity in terminology. Casual references to cases of pernicious anæmia in Asiatics in the literature should not, therefore, be accepted at their face value. However, from time to time claims have been made for the occurrence of true Addisonian pernicious anæmia in Indians; elsewhere in this number, Major Taylor and Dr. Chitkara state that 'in the Punjab true pernicious anæmia is not rare'.

The question now arises—What constitutes a case of pernicious anæmia? The disease has been recognized as a distinct clinical entity for many years, as a 'primary' anæmia with a high colour index, associated with achlorhydria and subacute continued degeneration of the cord. Recent work has added much to our knowledge of its aetiology and has removed it from the list of incurable diseases, but has done little to define the disease entity more clearly, or to separate it from any associated clinical types—except perhaps from achrestic anæmia, which probably has an entirely different aetiology—mainly because, as we have said, our clinical conception of the disease was already a clear one; another reason is the fact that in Europe and America a large majority of the macrocytic anæmias are Addisonian pernicious anæmia, but this statement is not true of the macrocytic anæmias in India and some other tropical and subtropical countries.

Pernicious anæmia is a disease of late middle life, more commonly of males, usually associated with symptoms of severe anæmia, gastrointestinal deficiencies, and involvement of the central nervous system; it is a disease that shows periods of remission and relapse, and, if untreated, ends fatally. Pathologically, it is a macrocytic hyperchromic anæmia, in which megaloblasts appear in the blood from time to time, and in which the bone marrow shows a characteristic megaloblastic activity. The van den Bergh reaction (indirect) is positive, and there is complete achlorhydria, even after histamine injections. Recent work has shown that not only are acid and pepsin absent from the gastric juice, but also the 'intrinsic factor', a substance which with the 'extrinsic factor', supplied in certain foods, forms a hæmopoietic principle that is essential for the normal maturation of red cells. This hæmopoietic principle is stored in the liver and complete remission of symptoms, except those due to permanent neurological changes, can be effected by administration of the liver extract. This hæmopoietic principle is present in a highly refined form in the so-called West and Dakin fraction of liver extract, which is supplied under a number of proprietary names, e.g., anahæmin, pernæmon forte and examen. The gastric defect is a permanent one and patients must continue to take liver by mouth or receive

liver-extract injections for the rest of their lives or the condition will relapse.

How far do the cases reported correspond with this description of the disease? The final criterion is the absence of the intrinsic factor from the gastric secretion. This can only be shown by the extremely complicated method of taking the gastric juice, adding the extrinsic factor, feeding the mixture to a patient with pernicious anæmia, and noting whether it causes a reticulocyte response or not. Such a procedure is out of the question in India; we must therefore be content with strong presumptive evidence.

It is generally accepted that the intrinsic factor will not be absent unless there is complete histamine-fast achlorhydria, but the reverse is not the case, for achlorhydria occurs in about 10 per cent of normal individuals.

The neurological changes in pernicious anæmia, though of frequent occurrence, are neither constant nor confined only to this disease, and the megaloblastic reaction in the bone marrow, which is constant in pernicious anæmia, also occurs in other macrocytic anæmias.

Response to anahæmin, with typical reticulocyte rise, is also suggestive, for it has been shown by Napier (*Lancet*, 1938 *ii*, 106) and Wills and Evans (*Lancet*, 1938 *ii*, 416) that Wills' tropical macrocytic anæmia does not usually respond to anahæmin, though it does to crude liver extracts: however, this again is not conclusive evidence, for Napier (*I. M. G.*, 74, 1) showed that some cases of macrocytic anæmia with normal gastric acidity do respond to anahæmin in large doses; this observation was confirmed by Foy and Kondi (*Lancet*, 1939 *ii*, 360) in Macedonia.

Finally, there is the permanence of the gastric lesions and the certainty of the return

of the signs and symptoms unless treatment is maintained. There is a tendency in many types of macrocytic anæmia, especially those associated with splenomegaly, for the anæmia to recur when the patients return to their previous mode of life after a year or so (Napier, *loc. cit.*), but in the case of pernicious anæmia deterioration will commence within one to two months of the discontinuance of treatment.

It therefore resolves itself into a mathematical problem of the frequency of the occurrence of these different findings. A case of recurring macrocytic anæmia in which there are neurological symptoms, complete achlorhydria, and a typical response to anahæmin is not necessarily a case of pernicious anæmia, for the neurological symptoms and the achlorhydria might be accidental associations, but, if such a combination turned up very frequently, one would have to associate it with the pernicious anæmia syndrome.

In Bengal, though we have been studying macrocytic anæmia at the School of Tropical Medicine for some years, we have only encountered cases that fulfilled these criteria amongst Europeans and Anglo-Indians, who form a very small percentage of our hospital cases. The position in the Punjab may be different, but we do not think that the evidence presented in the paper in this number justifies the statement that pernicious anæmia is not rare in that province.

However, we repeat, time has a way of levelling out differences in the distribution of diseases, and we shall be surprised if it is ever shown that the physiological make-up of Indians is such that they are entirely immune from pernicious anæmia, though we still believe that the disease is rare amongst them.

## Special Articles

### AN ACCOUNT OF INDIAN MEDICINE

BY

JOHN FRYER, M.D., F.R.S.

(1650-1733 A.D.)

By D. V. S. REDDY

Vizagapatam

JOHN FRYER, M.D. (Cantab.), F.R.S., may be rightly described as the most observant and learned of all the physicians and surgeons of the East India Company in the 17th century. He came out to India in 1673 and served at various settlements in this country and Persia till 1682. During his journey to his station, Surat, he visited Fort St. George and Masulipatam on the Coromandel coast, and Goa and

other places on the west coast. After returning to England in 1682 he published a learned and delightful book on India, 'A new account of East India and Persia,' which is the basis for this article.

#### MEDICAL TOPOGRAPHY

Bombay: Writing of Bombay, Fryer says that the president has his chaplains, physicians, chyrurgeons and domestics. He also refers to the sickly progeny of English women.

'This may be attributed to their living at large not debarring themselves wine and strong drink which, immoderately used, influence the blood and spoils the milk in these hot countries, as Aristotle long ago declared. The natives abhor all heady liquours for which reason they approve better nurses.'



Fryer also adds 'The English have only a burying place but neither church or hospital both which are mightily to be desired.'

Fryer notes the unhealthiness of Bombay.

'At first thought to be caused by *Bubsho*, rotten fish; but though that be prohibited, yet it continues as Mortal: I rather impute it to the Situation, which causes an Infecundity in the Earth, and a Putridness in the Air, what being produced seldom coming to Maturity, whereby what is eaten is undigested; whence follows Fluxes, Dropsy, Scurvy, Barbiers (which is a enervating the whole Body, being neither able to use Hands or Feet), Gout, Stone, Malignant and Putrid Fevers which are Endemial Diseases.'

Goa: Writing of Goa, Fryer refers to the Paulistines who enjoy the biggest of the monasteries at St. Roch.

'In it is a Library, an Hospital, and an Apothecary's Shop well furnished with Medicines, where Gasper Antonio, a Florentine, a Lay-Brother of the Order, the Author of the Goa Stones, brings them in 50,000 Xerephins, by that invention Annually; he is an Old Man, and almost Blind, being of great Esteem for his long practice in Physick, and therefore applied to by the most Eminent of all Ranks and Orders in this City; it is Built like a Cross, and shews like a Scraglio on the water.'

'We descended from this lovely spectacle to the "Spittle", where we found the Poor faring well from their Benefactors.

The forepart of their vespers to the "Natal", I spend at the King's Hospital; where their Care for the Sick is commendable, an handsome Apothecary's Shop furnishing them with Medicines; The Physicians here are great Bleeders, insomuch that they exceed often 'Galen's Advice, an deliquium, in Fevers; hardly leaving enough to feed the Currents for Circulations; of which Cruelty some complain invidiously after Recovery.'

On his next visit to Goa Fryer lodged at the house of a French physician in the camp of St. Thomas which the city overlooked.

Surat: 'This City (Surat) is very nasty by their want of Privies, and their making Door a Dunghill; yet never had they any Plague, the Heats evaporating, and the Rains washing this Filth away.'

Masulipatam: People were free from sickness during summer but from May, with cooling showers, air grew foggy and Empyemas and fluxes were rife.

Madraspatam:

'About this mount (St. Thomas) live a cast of people one of whose legs are as big as an elephant's; which gives occasion for divulging it to be a judgment on them as the generation of assassins and murderers of the blessed apostle St. Thomas one of whom I saw at Fort St. George.'

Fryer did not visit Delhi, Agra, or Hugli.

#### *Seasons and diseases*

'The Diseases reign according to the Seasons; the North blowing, Bodies are rendered firm, solid and active by exhausting the Serous Humours, ad Hyp. 17. Aph. Lib. 3 for which cause Dry Weather is more healthy than Moist, it hastening Digestion, and facilitating Excretion, when no Fevers that are treacherous root themselves in a deep Putrefaction. About the Variable Months they are miserably afflicted with Coughs and Catarrhs, Tumours of the Mouth and Throat, Rheumatisms, and intermitting Fevers; also Small Pox invades the Youth, as in all India, so here; In the extreme Heats, Cholera Morbus, inflammation

of the Eyes by Dust and the fiery Temper of the Air: In the Rains, Fluxes, Apoplexies, and all. Distempers of the Brain, as well as Stomach.'

#### *Description of some diseases*

Fryer relates that the Governor of Junnar called all his male children and gave the history of their maladies but the details are lacking.

Writing of Jehonna and Hohelia, Fryer adds interesting observations on the dangers and diseases of a long voyage of the times.

'A Blessing not to be passed by without a grateful Commemoration, when half the Fleet were disabled by Distempers acquired by Salt Meats, and a long Voyage without Refreshments; and must have suffered too for want of Water, had not they met with a seasonable Recruit.'

'The first care then was to send the Sick Men ashore which it is incredible to relate how strangely they revived in so short a time, by feeding on Oranges and Fresh Limes, and the very smell of the Earth; for those that were carried from the Ships in Cradles and looked upon as desperate, in a day's time could take up their Beds and walk; only minding to fetch them anights, that the Misty Vapours might not hinder the kind Operation begun on their tainted Mass of Blood, by these specifick Medicines of Nature's own preparing.'

Fryer also notes in the course of his visit to a port called Tanore in Malabar district the prevalence of filariasis and records faithfully the traditional lore concerning the aetiology of the disease.

'Of Christians here are not an inconsiderable number. Here are also those Elephant-Legged St. Thomeans, which the unbiassed Enquiries will tell you chances to them two ways: By the Venom of a certain Snake, for which the Jangies or Pilgrims furnish them with a Factitious Stone (which we call a Snake-stone) and is Counterpoyson to all deadly Bites; if it stick, it attracts the Poyson; and put it into Milk, it recovers it self again, leaving its virelency therein, discovered by its Greenness: As also by drinking bad Water (to which as we to the Air, they attribute all Diseases) when they travel over the Sands, and then lying down when they are hot, till the Earth at Night is in a cold sweat, which penetrating the rarified Cuticle, fixes the Humours by intercepting their free concourse on that side, not to be remedied by any Panacea of their Esculapian Sectators; it is not much unlike the Elephantiasis Arabum.'

Fryer refers to venereal disease in the Canareese Country:

'The Diseases here are Epidemical, unless Plague Veneris be more Endemial, for which at this Season they have a Noble and Familiar Remedy, the Mango (which they have improved in all it(s) kinds to the utmost Perfection) being a Sovereign Medicine; they are the best and largest in India, most like a Pear-Plum, but three times as big, grow on a tree nearest a plum-Tree; the Fruit when Green scents like Turpentine, and pickled are the best Achars to provoke an Appetite; When Ripe, the Apples of Hisperides are but Fables to them; for Taste, the Nectarine, Peach, and Apricot fall short; they make them break out, and cleanse the Blood, and Salivate to the height of Mercurial Arcanaes; and afterwards fatten as much as Antimony, or Acorns do Hogs; these and Sarsa being their usual Diet.'

#### *Critical review of Indian medicine*

In the course of his history of India under the particular heading 'Sciences', Fryer notes

that, while magic and judicial astrology, grammar and rhetoric, are held in high esteem, 'Elocution, Physick, Metaphysicks, are not out of their element: Their Philosophers maintain an Aristotelian Vacuity; nor are they quite ignorant of Medicks, though Anatomy is not approved wherein they lean too much on Tradition, being able to give a very slender account of the Rational Part thereof.'

'They are unskill'd in Anatomy, even those of the Moors who follow the Arabians, thinking it unlawful to dissect Human Bodies whereupon Phlebotomy is not understood, they being ignorant how the veins lye; but they will worry themselves Martyrs to death by Leeches, clapping on an hundred at once, which they know not how to pull off, till they have filled themselves, and drop of their own accord.'

'Chirurgery is in as bad a plight, Amputation being an horrid thing: Yet I confess it is strange to see, that what Nature will effect on such Bodies, Intemperance has not debauch'd.

'Pharmacy is in no better condition: Apothecaries here being no more than Perfumers or Druggists, at best; for he that has the boldness to practise, makes up his own Medicines, which are generally such Draughts, that if their own Energy work not, yet the very Weight must force an Operation.

'They pretend to understand the Pulse, but the Urine they will not look on. Midwifery is in esteem among the Rich and Lazy only; the Poorer, while they are labouring or planting, go aside as if to do their Needs, deliver themselves, wash the Child, and lay it in a Clout or Hammock, and return to work again.'

Again Fryer says of the Moormen of Surat:

'At their labours they seldom call midwives being pretty quick that way, though there are not a few, live well by that profession; known by tufts of silk on their shoes or slippers all other women wearing them plain. At the end of their quarantine which is 40 days after the old law, women that were Confined, enter the hummums to purify.'

'To Cup they use Venosoes, without Scarifications. They have good Escaroticks and Vesicatories, made by a certain Nut, the same they chop or mark their Calicuts black with instead of Ink.

'They apply Cauteries most unmercifully in a Mordisheen, called so by the Portugals, being a Vomiting with a Loosness; the like is done in a Calenture.

'Physick here is now as in former days, open to all Pretenders: here being no Bars of Authority, or formal Graduation, Examination or Proof of their Proficiency: but every one ventures, and every one suffers; and those that are most skilled have it by Tradition, or former experience descending in their families; not considering either alteration of tempers or seasons, but what succeeded well to one, they apply to all.

'The Tortoise bears the Vogue for altering the Blood; wherefore good in Scurvies got by bad Air and Diet in long Voyages, and for the running of the Reins by impure Copulation; for which 'tis used as an undoubted Cure, purging by the Genitals an Oily viscous Matter of a Yellow hew, if fed upon constantly for thirty days; restoring the decayed Vigour of the Body, and giving it a grace and lustre as elegant, as Viper Wine does Consumptive Persons, or worn-out Prostitutes.'

'In Fevers their method is to prescribe Coolers, till they have extinguished the Vital Heat; and if the Patients are so robust to conquer the Remedies used to quench the Flame of the Acute Disease, yet are they left labouring under Chronical ones, as Dropsy, Jaundice, and Ill Habits, a long while before they recover their Pristine Heat.'

### *Some home remedies*

Here they will submit to spells and charms, and the advice of old women.

Fryer also adds notes on simple home remedies like butter of 400 years' standing 'prized by gentiles as high as gold prevalent in old aches and sore eyes one of which (tank) was opened for my sake and a present made me of its black stinking viscous balsom'.

To correct 'distempers of the brain as well as stomach the natives eat Hing, a sort of liquid Assafætida, whereby they smell odiously. For all Lethargick Fits they use Garlick and Ginger, given in Oyl or Butter'. He also refers to the uses and popularity of 'Goa stones' in various diseases.

### *Indian doctors at work*

Discussing the inhabitants of India, he divides Brahmins into two chief sects, Butts and Sinais, the latter being fish-eaters.

'The Butts live a life of study abstracted from all worldly employments, unless such as are for saving and preserving of life, the chiefest and skilfullest physicians being of their tribe. The Sinais are more biassed by secular offices, farmers, governors of towns, physicians, accountants, clerks and interpreters.'

'I have seen a Barber undertake the Cure of Bloody Flux, by pretending the Guts were displaced, and laying the patient on his Back, and gently tickling his Reins, thrust on each side the Abdomen with all his strength; then placing a Pot filled with dried Earth, like that of Samos, upon his Navel, he made it fast by a Ligature; and on some Bodies thus treated he had gained Credit, but this died. Prosper Alpinus mentions something like this among the Egyptians.'

At Surat, Fryer took the help of a Brahmin skilled in simples to identify and learn the uses of various plants. The same person enlightened Fryer on ban and datura 'Here he discovered to me his beloved Alluh the bark of a tree the present remedy against all manner of fluxies' Indarjau? Rohun?

'Here is a Brahmin Doctor who has raised a good Fortune; they pretend to no Fees, but make them pay in their Physick; and think it Honour enough if you favour them with the Title of your Physician only.

This Brahmin comes everyday, and feels every Man's Pulse in the Factory, and is often made use of for a powder for Agues, which works as infallibly as the Peruvian Bark; it is a preparation of Natural Channaber.'

### *FRYER'S ARISTOCRATIC PATIENTS AND HIS STRANGE EXPERIENCES*

His medical services were in constant requisition not only in Surat and Bombay but also all over the west coast of India.

Joao Mendes, a wealthy Portuguese of Bassein, sent for him to attend on his only daughter, a handsome girl engaged to marry the Portuguese admiral of the North.

One of the Mogul's generals, who was also Governor of Jeneah (Junnar in Poona District), requisitioned Fryer's services. Gerald Aungier, chief at Bombay, commanded Fryer to render the necessary expert medical aid. On arriving at this place, a letter from President

Aungier, was handed over to Fryer. The communication described who the distinguished patients were but counselled Fryer to be patient till a good and auspicious day presented.

'A good day coming, the Governor sent for me to Visit his Lady in the Haram, which was opposite to a Chamber he sate in, accompanied only with one pretty Wanton Boy, his Only Son by this Woman; upon which account he had the greater kindness for her; An old Gentle-woman with a Tiffany Vail, made many trips, being, I suppose, the Government of the Women's Quarters: at least I was called and admitted with my Linguist.

'At our being ready to enter, she clapped with her Hands to give Notice; when we were led through a long dark Entry, with Dormitories on both sides, the Doors of which Creaked in our passage (but I was cautious of being too Circumspect) till we came to an airy Choultry; where was placed a Bed hung with Silk curtains; to which being brought, I was Com-manded to place by it, from whence I might conveniently Discourse and Feel her Pulse, putting my Hand under the Curtains. It was agreed among them to impose upon me; wherefore at first they gave me a Slave's Hand, whom I declared to be Sound and Free from any disease, nothing contradicting the true Tenor and Rythme of Pulsation; when they began to be more ingenious, telling me, it was done to try me; Then was given me another Hand, which demonstrated a weak languid Constitution; and collecting the Signs and Symptoms, I feared not to give Sentence; which met with their approbation, and so I was sent back the same way I came.'

#### A GOLDEN SHOWER OF PAGODAS FOR A VENESECTION

'The Caun had been acquainted with what had passed, and seemed pleased; whereupon I must visit the Haram again the next day to Bleed another of his Wives, he being tolerated Four, though he keeps more than three hundred concubines.

And now the Curtains was extended athward the Choultry, and an Arm held forth at an hole; but this was a slight fence for such Animals, who leaning too hard as they peeped, pulled it down, and discovered the whole Bevy, fluttering like so many Birds when a Net is cast over them; yet none of them sought to escape, but feigning a shamefacedness, continued looking through the wide Lattice of their Fingers: The Lady I had by the Arm was a Plump Russet Dame summoning the remainder of her Blood to enliven her cheeks (for among the darkest Blacks, the Passions of Fear, Anger, or Joy, are discernible enough in the Face) and she bearing a command, caused it to be hung up again; pouring upon her extravasated Blood a Golden shower of Pagodas, which I made my Man fish for.'

#### THE PLACE OF ELECTRO-SURGERY OF TONSILS IN INDIAN PRACTICE

By N. AHMED

*Divisional Medical Officer, East Indian Railway*

ELECTRO-SURGERY of the tonsils has assumed a definite place in oto-laryngology. There are no two opinions regarding its value, at least in those cases for which ordinary surgery is contra-indicated.

On 14th December, 1938, I sent a questionnaire to practically all the teaching institutions in India, Burma and Ceylon in order to ascertain what place electro-coagulation of the tonsils has in the practice of their attached hospitals, where young medical men receive

their training. The result of the investigation is given below. It has revealed a state of affairs which I consider needs attention. The copy of the questionnaire is given below :—

#### Electro-coagulation of Tonsils

by

Diathermy or Short-Wave Machine.

1. Name of Hospital—
2. Is it done at all in your Hospital?—
3. If yes, in which department—  
(a) Radiological—  
(b) Oto-laryngological—
4. Approximate number of cases treated in 1937-38.

The superintendents of the hospitals attached to 17 medical colleges and 27 medical schools were requested to supply the information :—

Amongst the 17 medical colleges two of them did not reply; ten replied 'No'.

Vizagapatam bought the short-wave apparatus in December 1938. Osmania Hyderabad said 'Yes but rarely', and gave no statistics. The Women's College, Delhi, replied 'Occasionally for tonsillar remains—none in 1937-38'.

It therefore comes to this that only 3 institutions attached to the medical colleges in India, Burma and Ceylon use electro-coagulation. They are the Grant and Gordhan Das Colleges in Bombay and the Medical College Hospitals in Calcutta. The cases they did were :—

J. J. Hospital, Bombay	..	8 in 1937
K. E. M. Hospital, Bombay	{ ..	6 in 1937
	{ ..	6 in 1938
Medical College Hospital, Calcutta.	{ ..	11 in 1937
	{ ..	8 in 1938

Amongst the 27 medical schools 14 did not reply; 11 of them replied 'No'. The only two, Agra and Darbhanga, said 'Yes' but Agra treated none in 1937 and only one in 1938, while Darbhanga did 3 cases in 1936 and none in 1937-38.

This being the state of affairs in the hospitals attached to the teaching institutions it would not serve any useful purpose to probe further into the question of what other leading hospitals in India are doing in the direction of fostering and promoting the advancement of electro-surgical methods in tonsillectomy. Whatever work is done in India appears to be wholly due to the individual efforts of the specialists and the enthusiasts amongst the general practitioners.

Apart from the question of training medical students, one wonders what happens to those patients whose tonsils are in need of removal, but for whom ordinary surgery is contra-indicated or to those who abhor or dread surgery and refuse it on account of the risk to their health, happiness and even life. To whom in India should go the aged, the very weak and debilitated, the tuberculous, the syphilitic, the hæmophiliacs, the invalids with serious kidney, liver, heart and pulmonary lesions, those with goitre, acute rheumatism,

inflamed septic tonsils or infected tonsillar remnants, the very nervous, who readily agree to anything but a knife, when their tonsils are in immediate need of removal?

It is my experience that the majority of the old practitioners, and not a very small proportion of the doctors who have recently qualified, if shown a diathermy machine are not able to say what it is.

After many years' experience, I am fully convinced of the very great scope and the extensive utility of the electro-coagulation of tonsils in Indian practice. I do not agree with those who advise against its adoption as a routine procedure. I see nothing in the method that warrants such an attitude. The only drawback, as far as the procedure itself is concerned, is its slowness, but, if a patient can afford the time, I see no reason why a doctor, who has the time, should insist on submitting him to the knife and its disadvantages and risks.

I realize the conditions that exist in big provincial hospitals. I do not blame a surgeon who is accustomed to use his knife and guillotine hesitating to adopt new methods when time is limited and the number of the patients great, but if he finds it convenient to use his knife or guillotine for reasons of his preference or the conservatism of the hospital organization and equipment, it is no fault of the coagulation and the method need not be condemned as unsuitable as a routine. I have actually experimented and found that 10 patients can be anaesthetized in half an hour, and not more than one hour would be taken for the day's coagulation of them.

The absolute limitations of the procedure are only two. Children under 6 years and the individual of any age and sex who will not open the mouth for even a few seconds for the work. During the period of six years I have seen only two such cases, a girl of 10 years and a lady of 22 years of age. The girl had

to be gagged and the lady needed patience to the point of exhaustion to get her to open her mouth and that also only on some days.

Electro-coagulation is an office procedure. It is easy, convenient and safe. It is my observation that Indian patients, educated or ignorant, bold or nervous, who are generally averse to the knife, very readily take to it, appreciate it, like it and after the experience of it have nothing but praise for it. Dan McKenzie, the famous oto-laryngologist writing on the subject, remarked—

'Little or no complaint is made and his endurance is never seriously taxed. He is, in fact, to continue the treatment from start to finish without leaving his work whatever it may be.....the disappearance of the slough takes place without the patient being aware of it.....so quiet and uneventful is the process, indeed, that even large tonsils seem to melt away almost imperceptibly.'

It is a pity that the premier hospitals are not giving a lead in using and popularizing this method, which has a great future in India.

The hospitals attached to all the medical colleges and schools in India could show a record of only 40 cases in two years in 1937 and 1938, while Dillinger in America put forward 2,200 cases of tonsils removed in 4 years by electro-coagulation and that too in 1926 to 1930.

The aim of this article is to urge the big hospitals to use the method and to let students be at least acquainted with it to the extent that they may in future be able intelligently to prescribe or actually use it for suitable cases in their practice.

My sincere thanks are due to the authorities of the hospitals, colleges and schools who so very kindly supplied me with the required information. I have also to thank Dr. S. C. Chatterji, the Chief Medical Officer, East Indian Railway, Calcutta, for permitting the publication of this article.

## Medical News

### TUBERCULOSIS WORKERS' CONFERENCE

THE first Tuberculosis Workers' Conference organized by the Tuberculosis Association of India was opened by Her Excellency the Marchioness of Linlithgow, the president of the Tuberculosis Association of India, in the Red Cross Conference Hall on the 20th November, 1939.

In requesting Her Excellency to open the Conference, Major-General G. G. Jolly, the chairman of the Tuberculosis Association of India, referred to a similar Conference held five years ago under the auspices of the King George Thanksgiving (Anti-Tuberculosis) Fund, the immediate predecessor of the present Association. The present Conference was the first to be held under the new Association founded by Her Excellency. This Conference met under circumstances when the finances of the anti-tuberculosis movement had been vastly augmented by Her Excellency's Appeal

for the King-Emperor's Anti-Tuberculosis Fund. Five years ago the total amount available to combat tuberculosis all over India was Rs. 9½ lacs, but to-day the collections had reached nearly Rs. 85 lacs. 'If the striking change in the finances of the movement against tuberculosis in India is any measure of the increased interest in the disease and of increased determination to tackle it, then the position is one which must give great satisfaction to all tuberculosis workers in India.' On behalf of the central committee and the delegates the chairman expressed his gratitude to Her Excellency for the honour she had paid them in coming to open the Conference. Her Excellency's presence, he said, was a demonstration of the active interest which, as president, she took in all the affairs of the Association.

Her Excellency in opening the Conference said:—  
'The Tuberculosis Association of India is the outcome of a resolution which I formed over three years ago

when, on my arrival in India, I asked for information about the disease in this country. The answer which I got was such that it convinced me that there was no time to be lost in starting a campaign to bring home to the people of this country the seriousness of the position.

'... I started an appeal forthwith with the result that to-day we are celebrating the first Tuberculosis Workers' Conference under the new Association.'

The promotion of these conferences was a function of the Central Association, and she hoped very much that they would take place at regular intervals to give the necessary opportunity for experienced tuberculosis workers from all over India to talk over points of importance with regard to the best measures of diagnosis and treatment of the disease. These discussions would be of the greatest value to the whole campaign in India by enabling the delegates of tuberculosis institutions and delegates representing other tuberculosis interests to improve their individual measures of diagnosis and treatment, and to give them new vision of some aspects of the whole tuberculosis problem.

Her Excellency wished that the Association could have offered the delegates to this Conference practical demonstrations with regard to diagnosis and treatment and hoped that when the model tuberculosis clinic in Delhi had been established it would be possible to do so at subsequent Conferences, and further expressed the hope that 'the Conference would succeed in giving to the delegates new knowledge, new experience, new vision and fresh vigour for the tremendous task that lay ahead of all of us in combating tuberculosis in India'.

Following Her Excellency's speech, Dr. Frimodt-Møller, the medical commissioner to the Tuberculosis Association of India, in his introductory remarks referred to the rapid development in the diagnosis and treatment of tuberculosis in recent years and to the necessity for all tuberculosis workers to come together for exchanging notes, thus benefiting from each other's experiences.

'There are questions in connection with diagnosis and treatment which cannot be solved without the opportunity of personal discussion amongst the tuberculosis workers in India. Such questions are those of standardization of records and definitions of types and stages of the disease, as well as of results of treatment, as many factors peculiar to India influencing prognosis and result of treatment must be taken into consideration before adequate terms of classification, prognosis and results can be decided upon.'

In a Conference of this nature not only must diagnosis and treatment be discussed but all such questions as 'environmental factors influencing the spread of the disease, the methods of discovering sources of infection and patients in the preclinical stage of the disease, vaccination of contacts and other important measures of prevention, all forming part of the work carried out from a tuberculosis clinic. Also other measures of prevention need discussion, as for instance the value in India of anti-tuberculosis legislation. Another series of questions to be considered were the relation of home-treatment and institutional treatment, the care and after-care of tuberculous patients including the questions of ex-patients' colonies and village settlements'.

Over fifty delegates from different parts of India attended the Conference. Papers on 25 different aspects of the tuberculosis problem were read and followed by lively discussions during the course of the Conference which lasted for four days.

In closing the Conference Her Excellency expressed her satisfaction at the valuable work that had been done and at the enthusiasm displayed by all concerned. She referred to the need for frequent conferences and hoped that all concerned would soon start preparations for the next.

A summary of the papers and discussions will appear in a subsequent issue of the *Indian Medical Gazette*.—  
Editor, J. M. G.

## BOMBAY MEDICAL COUNCIL

THE following extracts from a summary of the proceedings of the meeting of the Bombay Medical Council held on 4th September, 1939, are published for general information:—

The Council proceeded to consider a complaint against Major Raghunath Ganesh Dani, L.R.C.P., M.R.C.S., M.B., B.S., I.M.S. (Retd.), and Mr. Vishnu Raghunath Gosavi, L.R.C.P.S., regarding their running a private nursing home in Nasik designated 'Major Dani and Dr. Gosavi Maternity, Gynaecological, Surgical and Nursing Home' and issuing pamphlets, etc., and decided (i) that Major Dani and Mr. Gosavi be warned that they cannot call the nursing home after their names, *vide* rule 20 in section II of the Code of Medical Ethics, and (ii) that the publication of pamphlets and general distribution of annual reports is objectionable.

The Council proceeded to consider a suggestion made by the Executive Committee that it may be ruled that the Council will deal only with questions regarding registration, education and ethics and not with matters which concern the privileges of practitioners.

The Council proceeded to consider the reference from Government regarding the application of Mr. Ibrahim Sheikh Mohamedbhai Amin for permission to be registered under section 7 (3) of the Bombay Medical Act, VI of 1912, and decided to inform Government that in the opinion of the Council Mr. Amin be given the permission.

The Council proceeded to consider the reference from Government regarding the application of certain practitioners for the recognition for registration of their qualifications obtained between 1912 and 1916 from certain institutions not authorized to grant such qualifications under the Indian Medical Degrees Act, VII of 1916, and decided to inform Government that the Schedule to the Bombay Medical Act, VI of 1912, be amended so that those who qualified between 1912 and 1916 from the following institutions, *viz*—

the National Medical College, Calcutta,  
the College of Physicians and Surgeons of Calcutta,  
and

the International College of Physicians and Surgeons of India, Calcutta,  
be registered.

The Council proceeded to consider the reference from Government regarding the recognition of the medical degrees of the Tilak Maharashtra Vidyapeeth, Poona, for registration under the Bombay Medical Act, VI of 1912, and decided to inform Government that the diploma of Ayurvediya Visharad in Allopathy granted by the Tilak Maharashtra Vidyapeeth, Poona, up to 1936 be added to the qualifications recognized as registrable in part II of the Bombay Medical Register, section B.

The Council proceeded to consider the reference from Government regarding the amendment of rule 12 of the Rules of the Council and the voting paper given in the Appendix to that rule and decided that the following amendments to the rule and the Appendix to it be approved:—

I. After sub-rule (7) the following be inserted, namely:—

'(7-A) The President shall nominate as scrutineers such number of members of the Council not exceeding four, as he thinks fit.'

II. In the voting paper in the Appendix—

(1) The first column shall be deleted;

(2) (a) For the word 'Registrar' occurring at the right hand bottom corner the words 'Returning Officer' shall be substituted; and

(b) For instruction '4' the following shall be substituted, namely:—

'4. The elector shall enclose the voting paper in a small blank cover and then enclose that cover in a bigger cover in the left hand lower corner of which the elector shall write his full name and signature. If the elector fails so to write his full name and signature the voting paper shall be invalid.'



The Council proceeded to consider and approved an amendment to the travelling allowance rules of the Council so as to enable them to pay travelling allowance to members of Sub-Committees, etc., appointed by the Council or the Executive Committee.

The Council proceeded to hold an inquiry into the charges laid against Mr. Vishwanath Hari Bedekar, M.B., B.S., viz, (a) that he is conducting the birth control research bureau at 166A, Vincent Road, Dadar, where advice and treatment are provided in regard to the question of birth control and that treatment is given in the form of pills placed on the market by the Aryan Pharmacy, Vile Parle, in bottles labelled A. P. Brand B. U. C. and packed in boxes, (b) that he is thus using a secret remedy and associating himself in the manufacture and sale of a proprietary medicine and (c) that in relation thereto he has been guilty of infamous conduct in a professional respect, and it was decided that Mr. Vishwanath Hari Bedekar had been guilty of infamous conduct in a professional respect and the Registrar was directed to remove Mr. Bedekar's name from the Medical Register.

The Council proceeded to deal with the notice of a motion proposed to be moved by Mr. U. B. Narayanrao, L.C.P.S., to the effect that the courtesy title of 'Dr.' be used while addressing registered medical practitioners in all official correspondence but the President ruled the motion out of order.

The Council then proceeded to deal with the notice of a motion proposed to be moved by Mr. U. B. Narayanrao, L.C.P.S., seconded by Mr. V. D. Sathaye, B.Sc., L.C.P.S., to the effect that Government be requested to reconsider its decision regarding the continuation of the Bombay Medical Register in three sections as at present and to approve the previous resolution of the Council regarding the amalgamation of the three sections together and the motion was carried by a majority.

The Council proceeded to deal with the notice of a motion proposed to be moved by Mr. U. B. Narayanrao, L.C.P.S., seconded by Mr. V. D. Sathaye, B.Sc., L.C.P.S., to the effect that any qualification which is registrable and which is acquired without examination should have '(Hon.)' inserted after it in the Bombay Medical Register and the motion was carried by a majority.

The Council proceeded to consider the request of the Bombay blood transfusion service for the nomination by the Council of one of their members on the Committee of the Service and decided to appoint Mr. C. A. Amesur, M.S. (Lond.), M.R.C.S., D.L.O., as the nominee on the Committee.

The Council then proceeded to consider the question of appointing Visitors to attend and be present at the

Bombay University Medical Examinations and appointed Dr. Jivraj N. Mehta, M.D., M.R.C.P., etc., and Dr. P. C. Bharucha, M.D., B.S., as Visitors for the Examination in Medicine, the President (Major-General H. C. Buckley, M.D., F.R.C.S., R.H.P., I.M.S.), and Mrs. Tarabai Kotamrao, L.C.P.S., as Visitors for the Examination in Midwifery and Gynaecology, Mr. C. A. Amesur, M.S., M.R.C.S., D.L.O., as a Visitor for the Examination in Surgery, and Mr. C. J. Ghia, L.M. & S., M.L.A., and Mr. V. D. Sathaye, B.Sc., L.C.P.S., as Visitors for the Examination in Ophthalmology.

The Council proceeded to consider the reports of the Visitors to the examinations in Surgery, Midwifery and Medicine of the College of Physicians and Surgeons of Bombay and decided that the attention of the College be drawn to the remarks of the Visitors.

The Council proceeded to consider the request of the manufacturers, manufacturers' agents and importers of pharmaceutical and toilet preparations, Bombay, for the nomination by the Council of one member on the Board proposed by them to be formed to decide on the classification of spirituous preparations and the question of exemption of any preparations from the operation of the proposed prohibition legislation and it was decided that no member be nominated by the Council on the proposed Board.

The Council proceeded to deal with a motion made by Mr. U. B. Narayanrao, L.C.P.S., seconded by Mr. V. D. Sathaye, B.Sc., L.C.P.S., regarding the appointment of Visitors to attend and be present at the L.M.S. Examination to the Medico-Surgical College at Nova Goa and the motion was lost.

The Council proceeded to deal with the notice of a motion proposed to be moved by Mr. V. D. Sathaye, B.Sc., L.C.P.S., regarding (1) the deletion of certain qualifications such as L.C.P.S. (Bom.), L.S.M.F. (Bengal), L.S.M.F. (U. P.), etc., from the Schedule to the Bombay Medical Act, 1912, with a specified reservation in favour of those qualified before such alteration and the students who have already commenced their medical studies and (2) the appointment of a Committee to inspect the courses of studies or the L.C.P.S. Bombay examination and the facilities for the same at the Medical Schools and the motion was lost.

The Council proceeded to consider the appointment of the Registrar of the Council and the applications received for the post and appointed a Sub-Committee of Lieut.-Col. S. L. Bhatia, M.C., M.A., M.D., I.M.S., Dr. B. G. Vad, M.B., B.S., M.D., and Dr. Jivraj N. Mehta, M.D., M.R.C.P., etc., with instructions that the Sub-Committee's recommendations be circulated to the members of the Council and the result thus reached be forwarded to Government for approval.

## Current Topics

### Medical Treatment of Mustard Gas Casualties

(Abstracted from the *Air Raid Precautions, Handbook No. 3*, 1st edition, London, His Majesty's Stationery Office)

[We do not believe that the towns of India will ever be subjected to raids by enemy aircraft. Should such an unexpected event occur and high explosive bombs cause casualties amongst our people, many medical men, by the application of their general surgical knowledge, will be able to meet the situation, though special knowledge on the subject would be very valuable.

However, as the casualties caused by mustard gas are so far removed from our normal experience, and as the knowledge of how to deal with such casualties, which would be so vital in the unhappy event of this form of warfare being resorted to, cannot be acquired from ordinary medical or surgical textbooks, we feel

justified in devoting a few columns in this and in our next issue to this subject.

Those who feel that they would like further information on the treatment of air raid casualties are referred to the series of handbooks from which this abstract is taken, or to the pamphlets issued under the auspices of the Indian Medical Association by their able and energetic secretary, Dr. S. K. Ray, in which a useful résumé of these handbooks is given, or to the book reviewed in our July issue *Medical Organization and Surgical Practice in Air Raids*, by P. H. Mitchiner.—Editor, I. M. G.]

### Nature of Casualties from Mustard Gas Vapour

MUSTARD gas vapour can be harmful in concentrations that may not be readily noticed by the sense of smell; also, the sense of smell for mustard gas vapour tends to become dulled quickly, in which case the danger may no longer be appreciated.



The cumulative effect of repeated small doses of the vapour is another insidious danger.

The vapour concentration necessary to produce effective results need not be of a high order. One hour's exposure to a concentration of one part of mustard gas vapour in one million parts of air is sufficient to incapacitate an unprotected man for about two weeks, through conjunctivitis.

In the event of a mustard gas attack on a large town some persons who have actually been exposed to the gas may, owing to local conditions, be unable to get away from their places of business before the inflammation of the eyes has become severe. If for that reason they can no longer see they should be treated like blind persons and should be conducted to the first aid post, the hospital, or their homes, as the case may be. The personnel of the Voluntary Aid Organizations should be prepared to give their assistance in such cases, and it need only be pointed out that if this type of casualty is numerous it is possible to collect a small number of them into a party, each man holding on to his neighbour, when a single guide can lead the whole party.

The possibility of the odour of mustard gas being masked by smokes or the fumes from high explosive, and its lack of immediate sensory irritation in what are yet effective concentrations, are additional dangers.

The degree of severity of mustard gas vapour casualties naturally varies with the concentration and the period of exposure. The least severe case may only show light conjunctivitis, with almost no erythema of the skin and only a slight hoarseness of the voice; the most serious, on the other hand, may present a picture of the most profound illness, usually with widespread skin burns, severe eye effects and damage to the respiratory tract.

A moderately severe case of exposure to the vapour when quite unprotected will present a typical appearance in 24 hours, with eye symptoms predominating; general reddening of the skin occurs, most marked in the genital region where the excoriation of the skin may cause distressing irritation, while, at about the same time, the respiratory system begins to show signs of involvement by a partial loss of voice and by a troublesome cough.

In the last war, the death rate among well disciplined troops with effective respirators was low, approximately 2 per cent of the mustard gas casualties, but the death rate among those without the protection afforded by a satisfactory respirator was much higher. Fatal cases were almost unknown within the first 24 hours after exposure. Death occurred at any date from the second or third day in the most severe cases to the third or fourth week in the more lingering ones, the highest death rate being at the end of the third or fourth day after exposure; and almost all the deaths were due to secondary broncho-pneumonia.

The main features of mustard gas vapour casualties may be briefly summarized as follows:—

(a) An insidious onset, with a latent period of two to forty-eight hours according to the concentration of the gas and the duration of exposure.

(b) Injury to the eyes, varying from simple conjunctivitis of a temporary nature to a severe keratitis and secondary septic complications of grave character.

(c) Laryngitis, involvement of trachea and bronchi, and possibly necrosis of the mucous membrane, leading to severe bronchitis or broncho-pneumonia.

(d) Early nausea, or persistent vomiting, accompanied by epigastric pain.

(e) Erythema of the skin—early in the case of exposed areas or of hot, moist surfaces—which may proceed to vesication, and excoriation and may be followed by secondary septic infection.

(f) Slow healing of the blistered, devitalized areas and pigmentation of the ensuing scar.

The types of injury which might result from exposure to mustard gas vapour are summarized below.

#### (1) ACTION ON THE EYES

The eyes are usually the first to show signs of the irritant action of mustard gas vapour. Even so the

visible onset of injury may be long delayed, the latent period varying from two to forty-eight hours, according to the dosage; but, once established it usually develops with rapidity. The initial symptoms of smarting and irritation are soon followed by lachrymation, pain in the eyes and headache; swelling of the eyelids quickly supervenes and may be so extreme as to close completely the palpebral fissure, while the simple lachrymation becomes muco-purulent as a result of secondary infection, and blepharospasm and photophobia are marked.

Changes in the eyeball itself are equally rapid; the injection which marked the onset of ocular signs is followed by swelling and oedema, to such an extent that the conjunctiva at the intrapalpebral aperture may even project between the eyelids, forming a characteristic yellowish-white, opaque band on either side of the cornea. A similar swelling of the palpebral conjunctiva under the eyelids may produce two chemotic folds which add to the distressing appearance of the eye by projecting between the lids.

The cornea, in the early stages, is grey and hazy, the haziness fading off above and below where partial projection is given by the eyelids; its surface becomes blurred and lustreless and later exhibits a typical 'orange skin' appearance. Exfoliation of the corneal cells may occur and in the presence of trauma ulceration may follow which, if complicated by secondary infection, may lead to permanent opacities and impairment of vision.

In serious cases, the condition of the cornea calls for the most careful and regular examination—a difficult procedure in view of the intense photophobia and blepharospasm. Recovery is slow; the oedema gradually subsides and the corneal epithelium begins to regain its lustre; gradually a condition is produced which is the exact opposite of the original appearance that is to say, the inter-palpebral area previously a dead white is now once more vascular and goes through a period of injection, whilst the previously injected areas, protected by the eyelids, are regaining their normal tint.

In the absence of corneal ulceration or conjunctival adhesions no permanent after-effects are usually met with, but lachrymation and photophobia are liable to persist for some time, and neurasthenic conditions may supervene in susceptible individuals.

The experience of the last war, when eye casualties were produced by the vapour more often than by a direct splash of the liquid, showed that eye injuries fall into three main groups:—

(a) Mild cases, 75 per cent of the total, fit for duty, on an average, in two weeks.

(b) Intermediate cases, 15 per cent, recovery in four to six weeks.

(c) Severe cases with corneal changes, about 10 per cent recovery in two to four months. Of these only a very small minority sustained total loss or impairment of vision.

#### (2) ACTION ON THE RESPIRATORY TRACT

The toxic effects of mustard gas vapour on the respiratory tract are shown by an early rhinitis (almost simultaneous with the onset of the conjunctivitis), accompanied by sneezing and the discharge of a profuse watery secretion, soon to become muco-purulent.

The larynx is usually affected early, and hoarseness or aphonia is frequent. The laryngitis may be mild if exposure has been limited to a low concentration, but oedema and even sloughing of the vocal cords may follow exposure to a high concentration.

In a severe case, the laryngeal inflammation tends to be reproduced in the trachea and bronchi, when the dry irritating cough, originally complained of at the onset of the laryngitis, is replaced by a loose cough accompanied by profuse muco-purulent expectoration and pain behind the sternum. A rising temperature and pulse indicate the onset of a severe bronchitis which may be complicated by sloughing of the inflamed tracheal mucous membrane; secondary infection of the latter soon leads to the development of a broncho-pneumonia with cyanosis. Rarely, abscess of the lung,

bronchiectasis, or even gangrene of the lung may occur not as a direct result of the gassing by mustard gas vapour, but of the secondary bacterial invasion which follows.

In the great majority of cases, however, the lesion is confined to a bronchitis which clears up in the course of a month or six weeks, leaving no after-effects.

### (3) ACTION ON THE SKIN

Before describing the effects of mustard gas vapour on the skin it may be useful to mention some of the factors that influence the penetration of the gas or modify the severity of its action.

As in the case of liquid mustard gas, the vapour owes its penetrative powers to its ready solubility in the lipid constituents of the skin. The degree of skin burning which follows is accentuated if the exposed skin area be a highly sensitive and tender region such as the scrotum, or if it be a surface which is subjected to constant friction, as is the case in the neck, the wrist and the ankles.

If the exposed skin surface be bare, the attack of the vapour will be direct, and the result more rapid than if the skin be clothed. This temporary protection of clothed areas is due to the fact that ordinary porous clothing material absorbs the vapour and retards its access to the skin; but if such clothing be worn beyond the period of actual exposure, or if the exposure be prolonged, the vapour retained by the clothing will increase the severity of the resulting skin burns.

This temporary protection varies in duration according to the nature, texture, thickness and degree of humidity of the clothing. Thus, a thin openwork cotton garment in close apposition with the body surface will not greatly retard the access of the vapour to the skin, whereas thick close-woven material, such as serge and woollen clothing generally, will definitely do so, and may even save the area from burns provided it be discarded on leaving the contaminated area.

After the lapse of the usual latent period, which may vary from two to forty-eight hours after exposure to the vapour of mustard gas, an erythematous blush appears over the affected area and gradually deepens in intensity until the skin looks scorched. This redness is not unlike the eruption of scarlet fever, and is usually accompanied by only a slight degree of irritation. The erythema is most marked on the skin areas which are hot and moist; dense tissues like the scalp, the palm of the hand or the skin of the heel usually escape unless the concentration of the vapour be high and localized to that area, as, for example, from drops of liquid mustard gas on a cloth cap.

The affected area soon begins to show superficial blistering in the form of small vesicles which rapidly coalesce to produce large blisters full of a clear, yellow serum; on evacuating this fluid and removing the overlying epithelium, a raw, red, weeping surface is exposed. As a rule vesication is complete by the second day, but blisters may appear in crops for days following exposure, even though all contaminated clothing was discarded at an early stage. Systemic disturbance is absent, unless the burns are extensive and severe; interference with sleep, however, may be caused by the distressing itching which may accompany the developing burns. Very mild cases may show simply erythema, followed later by pigmentation with scurfy desquamation, the 'blister' stage being absent.

In severe cases the erythema may deepen to a dusky, almost violet tint, oedema of the skin is marked, and blisters appear in the dark background overlying a deep red or hæmorrhagic base. Such blisters progress slowly, and are very prone to sepsis owing to the serious devitalization of the tissues; ulceration is liable to spread beyond the limits of the blister, and healing is very slow. If sepsis occurs it adds to the severity and duration of all lesions; the necrosed tissues form an excellent medium for pathogenic organisms, and death may result if extensive or deep burns are thus affected.

The healing of an uncomplicated vapour burn is more rapid than one due to liquid mustard gas, but a common feature of all mustard gas burns is the long

time they take to heal. The chemical irritant seriously damages the vitality of the affected tissues, and all processes of skin repair are delayed.

The healing stage is characterized by a brownish or coppery pigmentation of the epithelial layers in the areas previously affected by the erythema. This staining, however, is superficial, and usually disappears with the normal desquamation of the superficial layers of the skin.

As a rule, after-effects are absent, and the scars resulting from vapour burns are shallow, but a chronic eczematous condition or a generalized furunculosis may, rarely, follow such burns and prove obstinate to treatment.

### (4) OTHER EFFECTS OF MUSTARD GAS VAPOUR

Apart from its direct action on the eyes, the respiratory organs and the skin, mustard gas vapour may indirectly, and mainly owing to secondary infection, produce signs and symptoms in more remote organs of the body:—

(a) *Alimentary tract.*—It has already been mentioned that an early nausea, or even vomiting, accompanied by epigastric pain, often occurs in vapour poisoning by mustard gas. This effect is due to the swallowing of saliva or nasal secretion impregnated with the gas. Although it may prove obstinate during the first day, it rarely persists for more than 48 hours; similarly, the accompanying epigastric pain is of short duration, and the intestines are not usually affected. There are no lasting after-effects, but a functional condition of persistent nausea or vomiting has been observed occasionally.

(b) *Urinary tract.*—Traces of albumin have been found in the urine of early fatal cases, most probably due to congestion from circulatory weakness and not as a result of the action of the gas on the kidneys. It is only in the late stages of fatal cases, and particularly in those instances where widespread septic burns have occurred, that renal complications have been noticed, such as an acute hæmorrhagic nephritis. Pain on micturition, however, and even retention of urine may result from a local oedema and vesication of the penis.

(c) *Circulatory system.*—Blood changes are not met with, and any alteration in the leucocyte count is due either to pneumonic complications or to sepsis of the skin burns. Apart from the effects of the general toxæmias of pulmonary sepsis no primary changes occur in the cardiac mechanism, but a functional condition of disordered action of the heart is not uncommon as a result of the gassing.

### Nature of Casualties from Liquid Mustard Gas

The great majority of mustard gas casualties in the last war were caused by exposure to the vapour emanating from collections of the liquid deposited by shells. Aircraft bombs, owing to their different methods of construction, can contain more liquid gas than shells of the same total weight, and in addition aircraft can discharge liquid mustard gas as spray. Casualties in future wars may therefore be of more serious types caused by contamination by the liquid itself.

Casualties from the liquid may result in the case of:—

- (i) persons in the open under falling spray;
- (ii) persons near enough to the burst of a bomb to receive direct splashes of the liquid; and
- (iii) persons who touch material objects which have splashes of the liquid upon them.

The types of injury which might result are summarized below.

#### (1) SKIN BURNS DUE TO THE LIQUID

(a) *On bare skin.*—Although liquid mustard gas is a direct irritant to the skin, the sensory irritation is not immediate; its high lipid solubility enables it to penetrate tissues rapidly, but hours may elapse before the clinical signs make their appearance.

Penetration is rapid, and this rapidity is enhanced by an elevated temperature of the skin, or under

hot weather conditions. Indeed, there is reason to suspect that constant exposure to heat as in tropical or semi-tropical countries, leads to the acquisition of some degree of sensitivity to mustard gas.

The initial signs and symptoms of a typical mustard gas burn are an erythema at the site of contact, often accompanied by some itching; the capillaries become engorged, and oedema, with thickening of the skin supervenes. The erythema deepens, and in severe cases may even assume a livid hue; a pale, parchment-like area makes its appearance in the centre of this erythematous zone, and a vesicle, tensely filled with clear, yellow serum, gradually forms. This vesicle is the result of an inflammatory exudation of fluid which may continue for several days, according to the depth of penetration of the liquid mustard gas; the exudate, however, contains no actual mustard gas.

If the liquid contamination of the skin be widespread, as in a smear or splash, the erythema is followed by the appearance of numerous small vesicles which gradually coalesce to form large blebs, the underlying area being raw and oedematous; such blisters may continue to develop in crops for several days after contamination.

There is no evidence that any of the liquid mustard gas finds its way into the general circulation. Apart from the itching—which may be most severe where warm moist parts of the body are affected—there is little or no irritation except some stinging while vesication is developing, and no pain follows the appearance of the latter. The danger of sepsis following, however, is a real one, especially if the blistered area be extensive, as the tissues affected are devitalized, and the blood supply is impaired.

In the absence of secondary infection no constitutional disturbance is usually noted, and primary shock is absent. Healing, however, is a slow process (partly because the blood supply has been damaged, and partly on account of residual mustard gas or its derivatives persisting in the tissues). The resulting scar, which is soft and pliable, often assumes a coppery pigmentation which disappears after a time.

(b) *On clothed skin.*—Drops of liquid mustard gas on clothed areas of the body act by virtue of the high concentration of vapour evolved, the warmth of the underlying skin naturally assisting the process. A gross contamination of the clothing, on the other hand, such as may be produced by splashes or by accidental spilling, may result in actual contact of the liquid with the skin, when the action of the vapour would be super-added to that of the liquid.

All ordinary clothing is pervious to liquid mustard gas; but it is obvious that penetration will be much more rapid in the case of the single thin cotton garment of tropical and sub-tropical countries than with the multiple layers of woollen clothing worn in temperate climates.

If the garments be damp or wet, small drops of liquid mustard gas will rapidly penetrate and burn the skin. Although no reasons can be given for this, it has been proved experimentally to be an accurate statement of fact.

## (2) EYE BURNS DUE TO THE LIQUID

Contamination of the eye by spray or splash represents one of the gravest dangers to which the body can be subjected in the presence of liquid mustard gas, as permanent damage will result.

The degree of discomfort which immediately follows contact of the liquid with the eye may be slight, and usually subsides; symptoms often commence within half-an-hour, however, and within an hour or two the eye is inflamed and the eyelids are swollen and painful.

The clinical signs are ushered in by profuse lachrymation and conjunctivitis, and the condition develops with great rapidity. The eyelids become painful, swollen and greatly thickened by oedema, the palpebral conjunctiva is red and oedematous and the cornea develops opacities, while the ocular conjunctiva becomes congested and shows signs of ulceration.

Intra-ocular tension is increased, pain and headache are severe and a muco-purulent secretion exudes from the closed eyelids. Photophobia and blepharospasm may be extreme, and great difficulty is encountered in examining the swollen and painful eye.

After actual liquid mustard gas contamination of the eye, large areas of the conjunctiva may readily be shed, and partial or complete loss of vision result from the extensive ulceration and subsequent scarring.

Persons who have suffered from severe liquid contamination of the eye are liable to a recurrence of the symptoms on the slightest abrasion even up to 20 years later. This is probably due to the devitalized condition of the eye.

## Observations on Five-day Quinine Treatment of Malaria

By J. P. SANDERS, M.D.

and

W. T. DAWSON, M.D.

(From *The Southern Medical Journal*, Vol. XXXII, July 1939, p. 693)

THE present work had its origin in a conversation between us in 1930. We were discussing the possibilities of research in general practice. We recalled that Sir James Mackenzie had said that there was much research that could be done only by the general practitioner, and that it was frequently the common conditions about which information was lacking. This led to consideration of malaria, that being one of the common diseases of large parts of Louisiana and Texas.

It was felt that only the treatment of malaria was susceptible of study with the resources available. We had been taught that the best mode of treatment of malaria was to give 10 grains (0.6 gram) three times daily for three or four days followed by 10 grains daily for eight weeks. We did not know of any noteworthy opposition to this plan of treatment, which was, and, so far as we know, still is, the only plan of treatment of malaria endorsed by the National Malaria Committee. In fact, the only departures from such a plan, that we were aware of, took the form of using at least initially even larger doses of quinine, 45 to 60 grains (3 to 4 grams) or even more daily. In spite of the fact that no group of malariologists has in recent years advocated even the initial treatment of malaria with larger doses of quinine than 30 grains (2 grams) daily, many physicians are probably using daily dosage much in excess of that figure. In connection with these studies, with the kind assistance of Dr. E. L. Sanderson, Superintendent, data were obtained by a group of co-operating physicians on 189 patients with malaria, treated in the Shreveport Charity Hospital during 1937; 65 were started on 10 to 20 grains daily, 84 on 30 to 40 grains daily, and 40 on 60 to 90 grains daily (table I). The reason for favouring large doses initially has been to bring the fever under control as soon as possible. But in the group of 189 cases mentioned there was no significant difference among the immediate results obtained at the three dosage levels. One may say that, so far as information is available, treatment with over 30 grains daily appears to add nothing, and involves unnecessary expense, discomfort, and with the highest daily dosages some danger of nephritis, amblyopia or even the possibility of fatal quinine poisoning. Sollmann states that the fatal dose of quinine is usually given as 8 grams (125 grains), though 30 grams has been survived.

High dosage with quinine is very disagreeable to many patients, and the long-continued use of any drug is difficult to secure when the patient already feels well, as is usually the case after a few days' quinine treatment of malaria. We were, therefore, led to consider, a test of a very short course of treatment. We settled on 10 grains (0.6 gram) daily for four days,

TABLE I

*Influence of daily dosage of quinine on duration of fever (99°F. or over) after initial dose of quinine. Hospital patients*

Duration of fever in hours	BENIGN TERTIAN			ESTIVO-AUTUMNAL		
	Daily quinine dosage in grains					
	10-20	30-40	60-90	10-20	30-40	60-90
72 or less ..	10 14	9 11	5 9	13 18	12 21	9 15
24 or less .	15	12	10	25	24	17
48 or less ..						
TOTAL ..	15	12	10	25	24	17

and work was done for several years chiefly on quinidine.

Quinidine was brought into the picture because patients with quinine idiosyncrasy may tolerate quinidine, and we were interested in the possibility of using quinidine as a quinine substitute in malaria. In trying to obtain from the literature information about the antimalarial value of quinidine, we found that the Madras Cinchona Commission of 1866-68 had employed all four common cinchona bases extensively in treating malaria. Through the kindness of Mr. Bernard F. Howard, of Messrs. Howards and Sons, Ilford, England, a copy of their report was obtained. The most striking thing to us in this report was the subreport of Assistant Apothecary Wade, who treated 284 cases with quinine, 300 with quinidine, 'each dose being invariably taken in my presence'. Wade found that with either quinine or quinidine, in 88 cases out of 100, one dose (usually of 10 grains) sufficed to end the fever, about 11 per cent required a second dose and less than 1 per cent required any further treatment 'to abate the fever', which often remained absent for a long time. This work was, of course, done prior to the discovery of the malarial parasite. For a controlled study of the effects of a single day of quinine treatment, the reader is referred to the recent paper of Boyd and Kitchen. Reading over Wade's report, it seemed to us justifiable to try a single 10-grain dose daily for four days, and repeat treatment as needed. Nevertheless, it was an anxious time at first; an amount so small as this seemed altogether insufficient to control an illness so severe in some instances; the patients were anxiously watched; but both quinine and quinidine soon demonstrated a remarkable potency in this small dosage even in patients who seemed desperately ill. Later the dose was given twice a day, but not because of accidents, rather because it was feared that an occasional case might need twenty grains daily.

It was a surprise to us when the League of Nations Malaria Commission recommended in quinine treatment of malaria 15 to 18 grains daily for 5 to 7 days. We had not known that others were experimenting along the same lines.

Up to the end of 1935, 1,349 cases had been given quinidine treatment, and only 81 quinine. During the past two years work on quinine has been resumed, and a more extensive comparison made of quinine and quinidine. It is well known there are strain differences in response to treatment. Thus, in India quinine has appeared very effective in terminating attacks of falciparum (estivo-autumnal) malaria, but quinine treatment has proven not nearly so successful against some Italian strains of the same parasite. Our experience is that either quinine or quinidine treatment has been very satisfactory against such strains of malarial parasites as are met with around Shreveport, Louisiana, and in the few malaria patients hospitalized in the

John Sealy Hospital in Galveston, where malaria is not endemic.

TABLE II

*Follow-up on 46 non-hospitalized patients given short quinine treatment for malaria in the fall of 1936*

Daily dose in grains	For days	Number of cases	Relapsed * in 1936	Relapsed * in 1937	Relapsed * in 1938
10	5	23	3	6	4
20	5	23	1	3	5

\* Reinfection cannot be excluded.

TABLE III

*Follow-up on 349 non-hospitalized malaria patients given 20 grains daily for 5 days for malaria in 1937*

Smear diagnosis	Treated	Relapsed * in 1937	Relapsed * in 1938
Benign tertian ..	97	33 (28%)	19 †
Estivo-autumnal	117	22 (23%)	8 †
Negative ..	135	5 (4%)	16 †

\* Reinfection cannot be excluded.

† Follow-up included 324 of 349 1937 cases.

Patients treated with short courses of quinine, repeated as needed, in most cases appear, as with quinidine also, to require very little subsequent treatment (tables II and III). There seems, moreover, little difference in effect of 10 and 20 grains daily in this respect (table II). The actual percentage of relapses we cannot determine, since the patients treated continue to reside in the area in which they contracted malaria; it is, however, considered not heavily infected. We may reasonably estimate the percentage of relapses within a year as about 25 to 45 per cent, which actually includes clinical attacks of malaria during the rest of the year, during which the first course of treatment was given, and during the following year, except that for 1938, data are not given beyond 15th October. Almost the whole of the malaria season (May to October, inclusive) for this region is thus included. The estimated relapse percentages are probably too high rather than too low, especially as patients showing at clinical relapse a negative blood smear, or a different species of parasite from the initial infection were counted as relapse cases.

The repetition of the short course is effective; the parasites do not appear to become tolerant drug-resistant or 'host-resistant'. Whether or not this is because the courses of treatment given are very short, we do not know. The Malaria Commission of the League of Nations in its fourth general report is said to state with regard to quinine treatment that 'ill effects may occur when treatment is unnecessarily protracted'.

Examination of table III reveals a very interesting fact about the group of patients with negative blood smears, the so-called 'clinical malarials'. The number of relapses in this group is significantly less than in either the benign tertian or estivo-autumnal group. This is probably due, in the light of Bispham's report, to the fact that many of the 'clinical malarials' did not have malaria.

#### DISCUSSION

Our results are in general similar to those obtained in Europe, as set forth by Hackett. The results of our investigation of the effect of a 5-day treatment of malaria with quinine sulphate 10 or 20 grains daily for 5 days are briefly: (1) that the fever is subdued

as rapidly as by larger dosage, (2) that the percentage of relapses within a year may be estimated at 25 to 45 per cent. We have seen no reason to doubt that Bass is correct in calling for not over 30 grains daily in the beginning of treatment. With regard to duration of treatment, whether to advise continuance of 10 grains daily for eight weeks after the fever has subsided, or to advise stopping treatment at the end of 5 to 7 days, and resuming only if relapse occurs, we have nothing from our own data to guide us. After due consideration we rejected the plan of comparing the long treatment directly with the short treatment, because we could not feel sure that the patients on the long treatment would really continue to take the drug. We can only refer to the publications of the Malaria Commission of the League of Nations and to the excellent summary of Hackett, who favours the short treatment repeated as necessary. Hackett states that when this was tried in Sardinia on 300 non-hospitalized cases, the relapse rate after the long treatment was 40 per cent and after the short 46 per cent. 'It certainly did not compensate for the extra labour and expense involved in bullying apathetic villagers into swallowing quinine daily for two months.

#### CONCLUSIONS

(1) Relapses within a year following treatment of malaria with 20 grains quinine sulphate daily for five days are estimated as 25 to 45 per cent.

(2) The immediate effect against malarial fever of 10 to 20 grains quinine daily appears as good as that of larger doses.

(3) It is recognized that there are strain differences in response to quinine treatment; hence these conclusions apply strictly only to the area in which the work was done; but trial of the short course quinine treatment in other parts of the United States seems entirely justifiable.

### Complications following the Use of Ergotamine Tartrate Their Relation to the Treatment of Migraine Headache

By THEODORE J. C. VON STORCH, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXI, 23rd July, 1938, p. 293)

IN the past five years ergotamine tartrate has been used by an increasing number of physicians as an effective means of aborting or terminating migraine headache. More than 300 cases have been reported in which its use has given prompt relief in approximately 90 per cent of the patients. Many of these patients have continued to use ergotamine tartrate over long periods of time. Possible development of ergotism from such prolonged use has been a source of some concern. Accessory symptoms following the administration of ergotamine have occasionally alarmed practitioner and patient alike. Several recent reports of gangrene or death following the use of ergotamine tartrate in conditions other than migraine have tended to increase this anxiety. To date not a single case of gangrene following the use of ergotamine tartrate in migraine has been reported despite the fact that the literature contains references to more than 300 cases in which it has been used.

Analysis of the literature reveals that overdosage, sepsis, obliterative vascular disease and associated cardiovascular disease have played an important rôle in the production of the ill effects attributed to the use of ergotamine tartrate. Death occurred in only one case unassociated with any of these factors. In that case ergotamine tartrate had been administered into the uterine wall during a Cesarean section. Gangrene followed by spontaneous recovery occurred in three cases. Two were considered to show signs of impending gangrene. In the remaining two cases symptoms merely developed which unduly alarmed the physician. Many patients appeared to have a

pre-existing vasospastic tendency. Despite the presence of significant predisposing factors in the majority of cases, there remain a few cases in which, from the reported evidence, ergotamine tartrate must be considered responsible for the ill effects that followed its use.

Since there are no figures available with regard to the number of cases in which ergotamine tartrate has been used without untoward sequelæ, the percentage of such sequelæ may be only roughly estimated. However, such an estimate must be attempted in order that the number of accidents reported does not assume an undue importance. Judging from the amount of ergotamine tartrate dispensed in recent years for use in migraine headache, it is probable that at least several thousand patients have used it in America alone. In the past twenty years ergotamine tartrate has been dispensed in enormous quantities for use in obstetrics, gynecology and treatment of the thyrotoxicosis. In total, these cases could conservatively be estimated to run into the hundreds of thousands over this period. Therefore, the percentage of accidents over twenty years must be considerably less than 0.01 per cent (1 in 10,000). None of these accidents have occurred in the treatment of migraine headache.

#### CLINICAL OBSERVATIONS

In the past five years 550 patients with a presenting complaint of recurrent headache have been investigated by my associates and myself. About 430 of these patients were suffering from migraine headache. The diagnoses were established on criteria previously presented. All patients were suffering from recurrent headaches, and all presented at least two of the following three criteria: associated nausea and vomiting, visual symptoms, migraine headache in the immediate family. The group includes many of the so-called allergic, endocrine, gastrointestinal, hemispheric, menstrual, ocular and ophthalmic types and a few trigeminal and neuralgic varieties.

Of this group 189 unselected patients were treated by means of ergotamine tartrate. There were 159 females and thirty males. Regardless of type or presumed etiology 90.4 per cent of the patients were relieved of one or more attacks by one or more administrations of ergotamine tartrate.

Many of these patients have now used ergotamine tartrate in varying amounts from one to five years. Not many have been as faithful in keeping adequate records. Twenty patients who have kept adequate records were selected for presentation. These patients are those who have consistently taken the largest doses over the longest periods of time.

In none of these twenty patients have ergotism developed. As yet, there has been no evidence of ergotism in any of the 189 patients treated with ergotamine tartrate. No cases have been reported by other physicians using the drug in the treatment of migraine headache, nor have the American distributors of ergotamine tartrate been notified of any ergotism following its use in migraine headache.

A question of ergotism was raised in several of the cases. Repeated examination in these cases failed to reveal any evidence of acute or chronic ergotism and in all the use of the drug has been resumed without subsequent ill effect. In several of these, the suspected symptoms were discovered to have been present for several years before the use of ergotamine tartrate.

Although ergotism has not developed in these cases, accessory symptoms are frequent and occasionally disquieting. It is these symptoms which alarm the patient and physician. Some are identical with the symptoms of early ergotism. These require immediate investigation. A few suggest special sensitivity of certain organs or organ systems and may constitute warning of impending disaster. The majority are merely unpleasant concomitants.

Accessory symptoms associated with ergotamine tartrate therapy occur most frequently after its intravenous injection and less so after subcutaneous or intramuscular injection; they are infrequent when it is



given sublingually and least frequent when it is orally ingested. Unfortunately, the degree and rapidity of relief from headache vary in the same order, being most complete and rapid after intravenous injection and least so after oral ingestion.

The most commonly observed accessory symptoms are, in order of their frequency, nausea, vomiting, numbness or tingling of the hands and/or feet, muscle pains and stiffness (usually of the upper leg). Fatigue in varying degree occurred in most patients. None of these are cause for alarm. Nausea and vomiting, if severe, may be relieved in most cases by simultaneous sublingual or parenteral administration of from 1/150 to 1/120 grain (0.4 to 0.5 mg.) of atropine sulfate. Numbness and tingling are at times due to the use of ergotamine tartrate; at other times they are a component of the migraine syndrome unrelated to the use of ergotamine tartrate. These symptoms constitute a warning only when they become prolonged, persistent or progressive. In such instances, it is wise to discontinue ergot therapy, examine the patient carefully and resume therapy with caution if the examination has revealed no evidence of impending ergotism. Muscle pains and stiffness are frequent symptoms. They may be relieved by intravenous injections of suitable calcium compounds or more conveniently by massage and exercise. Lassitude and fatigue are not a source of much complaint except by those patients with associated neuroses.

Other symptoms occur in not more than 2 per cent of patients after the use of ergotamine tartrate. These are choking sensations, globus, insomnia, restlessness, substernal oppression, precordial pain, femoral or brachial perivascular pain, and pain in varicose veins. Of these, substernal oppression and vascular pain are most frequent. Following reassurance, the first two symptoms do not usually reappear with subsequent injections. The insomnia may be relieved by sedation when necessary. On the other hand, substernal oppression or precordial pain contra-indicates ergot therapy until coronary disease has been excluded. Treatment may then be cautiously resumed. No untoward results have followed its use in several cases presenting these symptoms. Vascular pain is not a contra-indication to its use unless obliterative vascular disease is present. Ergotamine tartrate has been used without disaster by a few patients complaining of pain in varicose veins. Whether or not it may be continued safely is as yet undetermined.

There are many symptoms which on rare occasions follow the use of ergotamine tartrate. Many of these would appear to be psychogenic, as, for example, generalized numbness, coldness and 'tightness', acute anxiety, and 'swelled head'. These symptoms have appeared in the more neurotic patients and usually do not reappear after reassurance. It is interesting that such symptoms may follow the use of ergotamine tartrate because it has been reported that this drug has been used to advantage in abolishing somewhat similar symptoms in psychotic patients. Urticaria, itching and local or generalized oedema have on rare occasions been observed to follow the administration of ergotamine tartrate. These symptoms raise the question of specific sensitivity, especially in the light of favourable reports concerning its use in the relief of pruritus of renal or hepatic origin. Numbness in one arm may rarely occur. Two patients reported cyanosis and paræsthesias of the face. Another complained of claw-hand twelve hours after oral administration of either 5 mg. of ergotamine tartrate or ergonovine. Mental dullness is a rare complaint. Even more rare are complaints of 'stiffness' of the jaw, neck or feet.

It is difficult to ascribe all the symptoms following the use of ergotamine tartrate to specific action of the drug. Many are undoubtedly psychogenic. Another large group may be ascribed to vasospasm. Among the latter are numbness, tingling and coldness of the extremities and vascular pains. Nausea and vomiting are probably the result of a specific action of the drug. Lassitude, fatigue and dullness may be central effects

Oedema and itching are possibly evidence of a sensitivity to the drug.

The significant symptoms are those indicating the development of ergotism (numbness, tingling, coldness, blanching or cyanosis of extremities), those suggesting coronary occlusion (precordial pain and oppression, pain or paræsthesia of the entire arm), and those warning of vascular occlusion (vascular pains, cyanosis, blanching, peripheral pain and paræsthesias). The persistent occurrence of such symptoms temporarily contra-indicates the use of ergotamine tartrate. An examination should be made at once. If no evidence of organic pathologic condition is demonstrable, the treatment may be cautiously resumed.

#### SYMPTOMS AND SIGNS OF ERGOTISM

Because of the infrequent occurrence of ergotism following the use of ergotamine tartrate, its signs and symptoms have not been clearly defined. The occurrence of ergotism following the use of ergotamine tartrate has always been determined by the symptoms that follow over-ingestion of whole ergot. There are in whole ergot other active constituents, such as histamine, which may mask or alter the toxic phenomena due solely to ergotamine tartrate. Nevertheless, although ergotamine tartrate may produce a type of ergotism different from whole ergot poisoning, familiarity with the latter is essential in estimation of the former.

Ingestion of excessive amounts of whole ergot may cause a gangrenous, a convulsive or a combined type of ergotism. The more common symptoms of gangrenous ergotism are general lassitude, mental dullness, vague lumbar pains, cramplike pains in the calves and dull burning pains in the extremities followed by intense waves of heat or cold with numbness finally supervening. The signs consist of moderate vomiting, swollen or inflamed feet (rarely hands), a livid cold skin over the extremities with the appearance of red or violet vesicles and cyanosis later turning black. Jaundice often occurs. The extremities become pulseless and the gangrene is dry and bloodless until infection is superimposed. When infected, the gangrene becomes moist. The legs are especially affected, the hands rarely. Gangrene is equally frequent in males and females but is often less severe in the latter. In pregnant women whole ergot is reported to produce gangrene before it results in abortion.

Since convulsions do not invariably occur in 'convulsive ergotism', it is suggested that 'neurogenic ergotism' may be a better term. In this type the outstanding symptoms are fatigue, 'heaviness of head and limb', 'giddiness', insomnia, restlessness, excitement, delirium, dementia, mania, impaired sight or hearing, pain and pressure in the chest, gastric pain, formication, 'pins and needles', numbness and 'hot and cold waves'. Paræsthesias usually occur in both hands and feet but may occasionally be unilateral. The signs include painful spasm of the face, throat or diaphragm; contractures of the hands; tonus, clonus and myoclonus; myopia or miosis, cataract; vomiting, diarrhoea and amenorrhoea. Pseudotabetic signs occasionally occur. Hemiplegias or paraplegias may also occur. Histologic examination of the tissues has revealed degeneration of the optic nerve and of the dorsal column and peripheral (lateral column) spinal cord. The cord changes simulate tabes dorsalis or more frequently the type of degeneration found in deficiency diseases. In fact, it has been suggested that 'convulsive ergotism' is determined by a coexisting vitamin-A deficiency. Many of the signs, symptoms and pathologic changes of convulsive ergotism may be due to malnutrition and to hypovitaminosis, since most of these cases have occurred in famine districts.

It has been reported that children are more susceptible to ergotism than adults. There have, however, been no reports of ergotism in children who have received ergotamine tartrate. No untoward reactions have occurred in children who have received it for migraine attacks.



If one compares the accessory symptoms which most frequently follow the use of ergotamine tartrate with the description of ergotism just given, it becomes apparent that the former are quite similar to the milder symptoms of convulsive ergotism. This suggests that the factor responsible for neurogenic or convulsive ergotism is concentrated in the ergotamine tartrate fraction of whole ergot. On the other hand, other ergot derivatives produce much the same symptomatology. Furthermore, ergotamine tartrate is capable of producing either type of ergotism in animals or man. It would therefore appear that ergotamine tartrate produces a type of ergotism as yet indistinguishable from that caused by whole ergot.

#### PATHOLOGY OF ERGOTISM

Experimental gangrene in animals and accidental gangrene in man caused by ergotamine tartrate are quite similar from the pathologic point of view. The vascular alterations are of primary interest. In general there is an arterial vasospasm primarily affecting the arterioles and smaller arteries, although the larger arteries may at times be constricted to a greater degree. Associated with this vasoconstriction there are various degrees of intimal oedema and hyperplasia, hyaline degeneration, thickening of the arterial walls, lymphocytic infiltration and frequent thromboses. The capillaries have been found to be dilated. Venous vasoconstriction is not as marked as the arterial but is present in varying degrees. Thickening of the venous walls also occurs and thromboses are frequent.

Although Spiro maintained that ergotamine tartrate could not be considered to be a vasoconstrictor and Straub claimed that gangrene due to it was the result of vasomotor paralysis, there is much recent evidence to the contrary. Unpublished observations in E. A. Carmichael's laboratory have shown that ergotamine tartrate acts as a vasoconstrictor on the sympathetomized blood vessels of the finger. Polák has shown that gangrene is hastened by section of the abdominal sympathetic chains. Unpublished results (Carmichael) have suggested that it acts as a mild vasoconstrictor on the normal vessels of human skin. In fact, recent observations have indicated that its therapeutic effect in migraine headache is the result of vasoconstriction of the branches of the external carotid artery. Experimental and pathologic evidence in animals and man has thus confirmed the impression that at least gangrenous ergotism due to ergotamine tartrate is a vasospastic obliterative process.

An uncomplicated gangrene due to ergot is a dry gangrene until sepsis supervenes. Many cases of puerperal gangrene have been reported with and without ergot therapy. It is to be emphasized that these are usually moist and not clearly due to ergotamine tartrate.

Changes in the cord simulating those found in tabes dorsalis and the deficiency diseases have been reported in epidemics of ergotism. The only change in the nervous system so far reported after ergotamine tartrate is vacuolization of the myelin sheaths of the peripheral nerves.

It has been reported that an attack of ergotism sensitizes subjects to subsequent ingestion of ergot. There is no evidence that this is true of ergotamine tartrate or that a tolerance toward ergotamine tartrate is developed after its prolonged use.

#### TREATMENT OF ERGOTISM

The various means of treating ergotism indicate that no really efficient method has yet been devised. Obviously, the first and most important part of any treatment is that the patient should avoid ergot in any form. Various vasodilators have been used, such as amyl nitrite, sodium nitrite, glyceryl trinitrate and scopolamine hydrobromide. Atropine sulphate has been recommended. Theophylline compounds have been used, usually with scopolamine hydrobromide. Daily intravenous injections of from 15 to 20 c.c. of a 3 per cent solution of magnesium sulphate have been considered superior to the usual narcotics and bromides.

Barger lists the use of from 5 to 25 c.c. of 25 per cent magnesium sulphate intravenously. Intravenous dextrose may be used because of the hypoglycemia often present in ergotism. Chloroform, cardiac stimulants and emetics have been recommended when indicated. Because of the immunity in female rats to gangrene caused by ergotamine tartrate following the use of oestrin (theelin), intramuscular injections of oestrin (theelin, amniotin, theelol, progynon and the like) might be tried in the milder cases occurring in women. Alternate hot and cold foot baths or alternate suction by means of a 'vasculator' may be used for gangrene. As in many disorders, the best treatment for ergotism is prevention.

#### CONTRA-INDICATIONS

Just why sepsis should predispose to gangrene is not clear. In intravascular infection, such as thrombophlebitis, the relationship is more apparent. Several authors maintain that ergotamine tartrate is no more than a contributory agent to the production of gangrene in such cases. Others believe that it plays no rôle whatever in the production of gangrene in the septic puerperium. Nevertheless, because of the frequent presence of pre-existent sepsis in those cases wherein gangrene has followed the use of ergotamine tartrate, infection must be considered a contra-indication to the use of ergotamine tartrate in the treatment of migraine headache.

In order to prevent vascular occlusion and gangrene, ergotamine tartrate should not be used in the presence of Raynaud's or Buerger's disease, venous thromboses, syphilitic arteritis or marked atheromatous arterial disease, especially in cases presenting any degree of coronary occlusion. In several cases of essential hypertension, ergotamine tartrate has been used without disaster. It has also been safely used in several cases of arteriosclerosis and hypertension. Furthermore, there are reports concerning its use in Raynaud's disease. Experimental and pathologic evidence, however, indicates that, although capillaries may be dilated after overdoses of ergotamine tartrate, arteries and arterioles are constricted and obstructed. Therefore, because of experimental, pathologic and clinical reports concerning certain vasospastic and obliterative tendencies of ergotamine tartrate, it is considered unwise to use it in the presence of obliterative vascular disease, especially coronary occlusion.

Hepatic disease was present in four cases and renal malfunction in another four cases in which accidents followed the use of ergotamine tartrate. It may be that impairment of 'hepatic detoxication' or renal elimination allows some potentially dangerous component of ergotamine tartrate to act in an unrestrained fashion. As jaundice often occurs in whole ergot poisoning, it is possible that ergotamine tartrate may produce further hepatic damage in these cases. On the other hand, at least ninety patients with demonstrable hepatic disease have been treated with ergotamine tartrate with only four accidents. In the treatment of migraine headache, administration of ergotamine tartrate has been avoided in patients with demonstrable hepatic or renal disease. It is recommended that ergotamine tartrate be used cautiously, if at all, in the treatment of migraine headaches complicated by demonstrable hepatic or renal disease.

It has just been recommended that ergotamine be avoided in the treatment of migraine complicated by vasospastic and hepatic disease. Some authors maintain the migraine itself is a vasospastic disease, others that it is hepatic. How then can one use ergotamine in its treatment? No evidence for gross hepatic malfunction in migraine has been presented. There may be some barely detectable malfunction in a certain group of cases. This does not constitute a contra-indication to the use of ergotamine. As to vasospasm, no worthwhile evidence has been presented that vasospasm occurs in migraine to any degree. Certainly it is not the intracranial etiologic agent.

Several instances of chemically demonstrable vitamin-C deficiency have been observed in the present series

of migraine patients. Accessory symptoms following the use of ergotamine tartrate appeared to be much more severe than in the remaining patients. Possibly the action of ergotamine tartrate on the vascular and nervous systems of these patients is enhanced by the pre-existing pathologic changes due to the deficiency of vitamin C. The question is as yet unsettled.

A few patients may be hypersensitive to ergotamine tartrate. Such subjects give clinical evidence of extremely unstable vasomotor systems. In them marked and sometimes bizarre reactions occur following the use of ergotamine tartrate. Such conditions need hardly be listed as contra-indications, since the patients almost invariably refuse further ergotamine tartrate. It is essential in such cases to be certain that these patients are not denied treatment because of purely psychogenic symptoms. Several cautious and well controlled trials of ergotamine tartrate are indicated.

Despite observations that it is difficult to produce abortion with ergotamine tartrate, pregnancy must be considered a contra-indication to its use in migraine attacks. Fortunately, many women cease to have attacks after the first month of pregnancy.

#### DOSAGE

Overdosage appears to be responsible for most of the ill effects that follow the use of ergotamine tartrate. On the other hand, large doses have been used without ill effect. Lichtman has successfully used 1 mg. three times a day by mouth for twenty-eight days. Podolsky has used the same dose for fifty-six days at a time. Baber and Tietz have used 6 mg. a day for fourteen days and Meakins and Scriver have used up to 18 mg. a day for at least ten days. Brack is reported to have used 1 mg. three times a day for six months. Almost every obstetrician has used as many as two 0.5 mg. injections in one day, and I have on rare occasions used two such injections in one day. Five years' experience with the drug, however, has suggested that smaller doses are sufficiently effective.

In the treatment of migraine attacks, it is recommended that the intravenous route be used only by those thoroughly familiar with the drug. When administered by the intravenous route no more than 0.25 mg. (0.5 c.c.) is to be given at the initial trial. The maximum single intravenous dose is 0.5 mg. (1 c.c.). No more than one such injection should be given in twenty-four hours, nor more than two such injections in any one week. Continuance should not be at a rate greater than 0.5 mg. (1 c.c.) per week.

By way of the subcutaneous or intramuscular routes, the initial dosage may be increased to 0.5 mg. (1 c.c.), but the remainder of the precautions suggested for intravenous therapy apply as well to these methods of administration. Rarely two 0.5 mg. injections may be necessary within twenty-four hours. Two injections a week have been used by a few healthy patients without untoward effects.

Sublingually the dosage is much larger. The average patient requires from 3 to 4 mg. (three to four tablets) at the onset of a headache with from 1 to 2 mg. (one to two tablets) per hour thereafter, if necessary, until not more than a total of 10 mg. has been absorbed. Such a procedure may be followed safely once a week and possibly twice a week, if under the immediate care of a physician.

The average oral dose for ingestion is from 4 to 5 mg. (four to five tablets) taken at once, followed by 2 mg. (two tablets) an hour, if necessary, until a total of 11 mg. has been taken. When more than 8 mg. is necessary for relief by either the sublingual or the oral route, it is best to substitute the subcutaneous injection of 0.5 mg. (1 c.c.).

In the treatment of migraine headaches, it is essential that the drug be given as early in an attack as is possible, preferably during the prodromal stage. When given early, the amount necessary to produce relief is greatly decreased.

These precautions are considered to be entirely safe but practical. It should rarely be necessary to exceed such doses.

#### CONCLUSIONS

The reports of forty-two cases were found in the literature in which ill effects followed the use of ergotamine tartrate. The great majority of these occurred because of overdosage, pre-existing sepsis or obliterative vascular disease. These cases are conservatively estimated at not more than 0.01 per cent of the total number of cases in which ergotamine tartrate was used. No accidents have been reported following its use in the migraine syndrome.

In five years' experience no serious complications have occurred in the treatment of 189 patients with migraine headache. Accessory symptoms are frequent after the administration of ergotamine tartrate. Usually they are merely annoyances; occasionally they constitute warnings of impending disaster.

Contra-indications to the use of ergotamine tartrate are septic states, especially when associated with intravascular foci and obliterative vascular disease, especially when coronary.

Treatment should be continued with caution in the presence of marked arteriosclerosis, hepatic or renal disease, vitamin-C deficiency and hypersensitivity to the drug.

Overdosage has been regrettably frequent in the use of ergotamine tartrate in the treatment of conditions other than migraine. When correctly administered in the absence of contra-indications, ergotamine tartrate may be considered a safe and extremely valuable means of aborting or terminating migraine headaches.

#### Chemotherapy of Pneumococcal Pneumonia

By COLIN M. MACLEOD, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXIII, 7th October, 1939, p. 1405)

THE ideal chemotherapeutic agent may be defined as one which, by inhibiting certain vital functions of the invading micro-organism or neutralizing its products, terminates the disease without causing any toxic effect on the host. This definition presupposes that the point of attack must be on a specific function or structure unique to the micro-organism, so that the tissues and organs of the host escape the toxic action.

Ethylhydrocupreine (optochin) was introduced by Morgenroth and Levy in 1911 for the treatment of pneumococcal infections, after study of numerous other quinine derivatives. A good deal of enthusiasm followed the early experimental results and ethylhydrocupreine was used in the treatment of human pneumonia. However, the observations of Moore and Chesney led to the conclusion that the use of ethylhydrocupreine in the treatment of pneumonia could not be recommended since it was impossible to administer an amount sufficient to achieve an effective concentration in the blood stream without subjecting the patient to the danger of toxic effects, of which amblyopia was the most frequent. Other quinine derivatives have since been recommended but up to the present time not one has had widespread clinical use.

The report by Domagk in 1935 of the therapeutic action of a sulphonamide compound on infections due to the hæmolytic streptococcus led to the use of related compounds in the treatment of pneumococcal infections. Sulphanilamide was the first of these derivatives to be extensively used but its effect on experimental pneumococcal infections was found to be relatively small.

The most promising sulphonamide derivative, sulphapyridine, was introduced in England in 1938. The first report by Whitby on the use of this drug in experimental pneumococcal infections of mice showed such striking results that little time was lost in applying the experimental results directly in the treatment of pneumococcal infections of man. It is difficult to say at present how much the early enthusiasms may have to be tempered in the light of further experimental and clinical observations. However, it seems quite certain that the use of sulphapyridine is a distinct advance in the therapy of pneumococcal infections.

## MODE OF ACTION

The mode of action of the sulphonamide group of drugs on different species of bacteria is poorly understood. Sulphanilamide exerts a bacteriostatic effect on susceptible micro-organisms, but its mode of action has not been fully elucidated. It has been postulated that sulphanilamide achieves its bacteriostatic effect by the inhibition of certain enzyme systems of the bacterium, thus interfering with cell nutrition. On the other hand, it has been suggested that the drug combines with some essential growth substance, which then ceases to be available to the micro-organism. A somewhat different hypothesis has been advanced by Locke and his associates based on the observation that sulphanilamide when oxidized by ultra-violet rays exerts an anticatalase effect. From this point of view the action of sulphanilamide is indirect, depending on the accumulation of hydrogen peroxide when catalase is inhibited. In the case of micro-organisms such as the pneumococcus or the hæmolytic streptococcus, which do not possess demonstrable catalase activity, the bacteriostatic effect would then depend on the inhibition of catalase in the tissues and fluids of the host or in the medium in which the organisms are growing, thus permitting hydrogen peroxide to accumulate and exert a bacteriostatic effect. While this may be one of the systems affected by sulphanilamide or sulphapyridine, it would not appear to be the sole one so inhibited, since sulphapyridine will restrain the growth of pneumococci in a medium which does not contain demonstrable catalase.

## CLINICAL USE OF SULPHAPYRIDINE

The numerous reports concerning the therapeutic effect of sulphapyridine in pneumococcal pneumonia have been uniformly favourable. Mortality rates of from 2 to 10 per cent in series of cases reported from various parts of the world indicate that the drug is effective in reducing the mortality rate. However, insufficient attention has been paid to the toxic effects of this chemotherapeutic agent.

Nausea and vomiting are frequent accompaniments of the administration of sulphapyridine. These reactions are unrelated to the dosage of drug or to the blood level. Since vomiting occurs in individuals to whom the drug has been administered parenterally, the effect would appear to be central, in addition to a possible local action on the stomach. Morbilliform skin rashes have been reported, as well as numbness and tingling of the extremities. Cyanosis due to methæmoglobinæmia occurs, particularly if high blood levels of the drug are attained.

More serious toxic manifestations may appear, however, involving particularly the hæmopoietic system and the urinary tract.

## EFFECT OF SULPHAPYRIDINE ON HÆMPOIETIC SYSTEM

The occurrence of acute hæmolytic anæmia in patients receiving sulphanilamide has been the subject of many reports, but as yet there is little information available concerning increased blood destruction in patients receiving sulphapyridine. During the routine administration of sulphapyridine to patients with pneumonia, hæmolytic anæmia occurred in two instances; consequently a study of the effect of this drug on hæmolysis was undertaken. Estimation of the total urinary and fæcal excretion of urobilinogen was used as an index of the rate of hæmolysis, since by this means increases in the rate of blood destruction may be observed which might escape detection if only routine clinical procedures are used.

Of the twenty-six patients with pneumonia for whom estimations of urobilinogen excretion were made, six did not receive sulphapyridine and in none of these was there an increase in the excretion of urobilinogen. Twenty patients received sulphapyridine in total dosage varying between 4.5 and 81 gm. and in eight of these the excretion of urobilinogen in stools and urine was increased from one and one-half to five times the normal amount. Acute hæmolytic anæmia occurred in

three of these patients. However, in the twelve other patients who received sulphapyridine, the urobilinogen excretion was normal or only slightly increased. The total dosage of drug administered to patients in the latter group tended to be less than that given to patients who showed increased urobilinogen excretion.

Increased blood destruction does not appear to be a usual accompaniment of the acute infectious process itself, since in eighteen of the twenty-six patients studied the excretion of urobilinogen was within normal limits. The evidence indicates that hæmolysis was due to sulphapyridine rather than to pneumonia itself and that increased blood destruction occurs more frequently following the administration of this drug than would be suspected unless special methods for its detection are used.

The occurrence of granulocytopenia in patients receiving sulphapyridine has been reported. This toxic effect occurs less frequently than hæmolysis but is an additional reason for making repeated blood examinations on patients who receive the drug.

## EFFECT OF SULPHAPYRIDINE ON THE URINARY TRACT

The solubility of sulphapyridine is less than that of sulphanilamide. This may account in part for the occasionally erratic absorption of the former drug and also for irregularities in its excretion. Antopol and Robinson have described the occurrence of calculus formation in the urinary tract of monkeys fed sulphapyridine. The same complication occurred also in rats and rabbits, although in the case of the last two species much larger dosage was required. Renal calculi have been observed likewise by Gross, Cooper and Lewis in rats that were fed sulphapyridine. The calculi described by both groups of investigators were found to be composed chiefly of the acetyl derivative of sulphapyridine.

Hæmaturia, aside from that occurring during hæmorrhagic Bright's disease, has been observed in only two instances during the course of sulphapyridine therapy in this hospital. One of these patients, a man aged 21, suffered from typical renal colic with hæmaturia shortly after discontinuing the drug. A calculus was not visualized by x-ray examination and the symptoms gradually disappeared. According to Antopol and Robinson the concretions of sulphapyridine and its acetylated derivative which occur in the urinary tract of monkeys are not usually seen in roentgenograms although they may become radiopaque because of over-layering with calcium salts.

Southworth and Cook have reported the occurrence of azotemia in two of three patients who developed hæmaturia during sulphapyridine administration. In addition there was acute abdominal pain, which was believed to be of renal and ureteral origin. On cessation of drug therapy and with the forcing of fluids, these signs and symptoms cleared rapidly.

Depression of renal function may occur, however, in the absence of hæmaturia. In two patients treated with sulphapyridine we have observed a temporary depression of the urea clearance to critical levels associated with azotemia, although hæmaturia was not present in either instance. With discontinuance of drug administration there was a rapid improvement in kidney function with disappearance of azotemia, and complete recovery apparently ensued. The studies of Farr and Abernethy on renal physiology in lobar pneumonia indicate that depression of kidney function is not a usual accompaniment of this disease. Indeed, in the experience of these authors, patients below the age of 40 showed a marked elevation of the urea clearance during the acute phase of the disease, with persistence of the increased function for about one month. In the older age group the urea clearance showed little change.

The impression that the diminution of the urea clearance which occurred in the two cases noted may have been an expression of sulphapyridine toxicity is strengthened by the fact that acute hæmorrhagic Bright's disease has developed in two other patients who received the drug.

In the first of these patients the earliest symptoms of acute nephritis occurred during the time sulphapyridine was being administered. Although moderate dosage was used, the blood levels of sulphapyridine were abnormally high, associated with a sharp drop in urine output, which occurred within twenty-four hours after beginning treatment with the drug. Five days after the drug was withdrawn the patient's blood still contained 0.8 mg. per hundred cubic centimetres of free sulphapyridine. The occurrence of oedema, the elevation of blood pressure and gross abnormalities in the urine were of gradual rather than of acute onset. As far as could be determined, the renal function returned to normal in two months.

The course of events in the second patient likewise differs somewhat from the typical picture of acute nephritis complicating an acute infection in that the onset was gradual rather than sudden. The first urinary signs appeared on the day following the discontinuance of sulphapyridine therapy and for the succeeding fourteen days the symptoms increased in severity until the final explosive onset of acute uræmia associated with heart failure.

Only one patient received antipneumococcus serum treatment in addition to chemotherapy. The use of serum has not been associated in our experience with renal complications.

Both patients have recovered from the acute phase of nephritis, the first apparently completely, but in the second case only partial recovery has taken place during the four months since the onset of nephritis.

#### COMMENT

It may appear that undue stress has been laid on the toxic effects of sulphapyridine. However, it seems important that such effects should be generally recognized so that the caution may be observed in the clinical use of this valuable chemotherapeutic agent, not only as applied in the treatment of pneumonia but in other diseases as well.

Sulphapyridine gives promise of reducing the death rate from pneumococcal pneumonia and present indications make it seem probable that an even greater reduction in the mortality rate can be accomplished if the drug is used in conjunction with type-specific antipneumococcus serum.

In the opening paragraph of this paper the ideal chemotherapeutic agent was defined as 'one which, by inhibiting certain vital functions of the invading micro-organism or neutralizing its products, terminates the disease without causing any toxic effect on the host'. From this point of view sulphapyridine does not fully attain the ideal, since toxic effects of greater or lesser degree are not infrequent accompaniments of its clinical use. Moreover, this powerful drug may not necessarily inhibit the vital functions of the ordinarily susceptible invading micro-organism, since the virulent pneumococcus has the capacity both *in vivo* and *in vitro* to adapt itself so that the drug does not affect its rate of multiplication, virulence or specific immunologic structure.

## Reviews

**DISORDERS OF THE BLOOD: DIAGNOSIS, PATHOLOGY, TREATMENT AND TECHNIQUE.**—By Lionel E. H. Whitby, C.V.O., M.C., M.A., M.D. (Cantab.), F.R.C.P. (Lond.), D.P.H., and C. J. C. Britton, M.D. (New Zealand), D.P.H. Third Edition. 1939. J. and A. Churchill, Limited, London. Pp. xii plus 603, with 12 plates (8 coloured) and 61 text-figures. Price, 21s.

THIS is the third edition to appear within four years. We must refer our readers to previous reviews for details of the scope of this excellent book (November 1935 and December 1937). It was obviously the popularity of this book, which led to an early exhaustion of the issue, rather than the necessity for rewriting it that decided the publishers and authors to issue this new edition. It has however been extensively revised throughout and 18 pages have been added.

The problem in new editions is not what shall be added—because recent work usually dictates that—but what shall be omitted; this presents the real difficulty. Though we have not compared the editions page for page, we have not noticed any omissions that we regret; on the other hand, we would again draw the attention of the authors to the chapter on 'Infection and Infectious Disease', as being an excellent field for curtailment in the next edition: some of the misleading statements in this chapter, which is an unnecessary one, are a blot on the whole book.

In the preface to this edition the authors mention amongst other additional matter 'views concerning the technique and value of sternal biopsy as judged by our experience'. After the reviewer had gone through the process of looking up 'sternal puncture. See Bone marrow biopsy' and 'Bone marrow, biopsy *v. infra*' (it is a curious form of parsimony common to publishers that prevents them throwing in a page number in these circumstances), he found a score of references to bone-marrow biopsy including five under the sub-heading 'value of'. He hoped that at least one of these would be a general appraisal of the value of sternal puncture, but he was disappointed; this is nowhere given.

In the section on the technique of sternal puncture, there are a number of points with which the reviewer cannot agree. For example, the reason for not taking more than 0.25 c.cm. of fluid is surely not simply to avoid causing pain because the withdrawal of the first few drops causes suction pain and if the fluid is then withdrawn slowly the pain, though still occurring, is less intense; there is however a sound reason for taking only a limited amount of fluid and this is that the true bone-marrow fluid is diluted with blood and the percentage incidence of the cells altered if much fluid is withdrawn. Again the idea of using a hammer seems to the reviewer fantastic, as in a personal experience of several hundreds of sternal punctures he has never had the slightest difficulty in piercing the outer table of the sternum, even with old and blunted Salath needles; nor does he understand how one can feel the definite 'give', as described by the authors, if the needle is driven in with a hammer.

The reviewer apologizes both to the authors and to readers of this journal for occupying so much space with these trivial criticisms of a book which has been his 'bible' for four years and which is in his experience the best book on blood diseases in the English language.

L. E. N.

**PIONEERS IN ACUTE ABDOMINAL SURGERY.**—By Zachary Cope, B.A., M.D., M.S. (Lond.), F.R.C.S. (Eng.). 1939. Oxford Medical Publications. Oxford University Press, London, Humphrey Milford. Pp. xii plus 131. Illustrated. Price, 7s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta.

SURGERY of the acute abdomen is such a difficult subject that an historical survey from the days of the pioneers is welcome. Our best thanks are due to Mr. Zachary Cope for his instructive monograph on this subject.

It was not the intention of the author to present a complete history of the development of acute abdominal surgery. There are, however, several omissions in the



narrative, which it is impossible to overlook. If Lister was the father of modern surgery, then of all his contemporaries who developed his ideas, the first place rightly belongs to Theodore Billroth who will always be remembered as the pioneer of the surgery of the alimentary tract. In 1872, he made the first resection of the oesophagus and in 1881, the first successful resection of the pylorus for cancer. Yet his name is not even mentioned in this book!

Modern surgery would not have been possible without two innovations; in 1886 von Bergmann introduced steam sterilization of dressings and instruments, and in 1890 Halsted introduced rubber gloves. These are important landmarks deserving of mention. Wölfler's name, too, is not mentioned but it was he who introduced gastro-jejunostomy in 1881.

The printing and illustrations are excellent but there are a few errors in the index.

P. N. R.

**DIVERTICULA AND DIVERTICULITIS OF THE INTESTINE.**—By Harold C. Edwards, M.S. (Lond.), F.R.C.S. (Eng.). 1939. John Wright and Sons, Limited, Bristol. Pp. xii plus 335. With 223 illustrations, many in colour. Price, 25s.

THERE is little doubt that this book is destined to be regarded as an authoritative contribution on a section of abdominal surgery, which, important though it is, remains to a large extent obscure. An appreciative foreword is contributed by Mr. Gordon Gordon-Taylor 'full of confidence in the certain welcome that awaits its reception from his own profession'. It is certain that the reader will endorse this view.

This book consists of 335 pages and four sections, of which the first deals with congenital diverticula. The next section is devoted to the consideration of diverticula of the duodenum. It is the most lucid and complete description of the subject that we have ever come across. There are eight chapters and 70 pages in this section, the concluding chapters on the clinical features and operative technique will be greatly appreciated.

Section three, dealing with diverticula of the jejunum, consists of seven chapters and 53 pages. The historical survey, collection of material and radiological diagnosis bear witness to the author's industry and scholarship. The important subject of diverticula of the large intestine is fully discussed in the last and biggest section. It is no small praise to say that it will be found equally useful to the anatomist, physiologist, pathologist and the surgeon.

This work is in substance the Jacksonian Prize Essay of the Royal College of Surgeons for the year 1932, revised and brought up to date. It represents the result of the author's personal investigation of clinical cases, pathological specimens from both operation and post-mortem and x-ray examination of the alimentary tract. The printing, get-up and illustrations are excellent, reflecting great credit to the publishers. A complete bibliography and a useful index are appended.

P. N. R.

**PHARMACOLOGY, MATERIA MEDICA AND THERAPEUTICS.**—By B. N. Ghosh, M.B.E., F.R.F.P. & S. (Glas.), F.R.S. (Edin.). Fifteenth Edition. 1939. Hilton and Company, 109, College Street, Calcutta. Pp. xv plus 763. Illustrated. Price, Rs. 8-8 or 15s. Obtainable from Messrs. Scientific Publishing Co., 9, Taltala Lane, Calcutta

THIS is one of the oldest standard textbooks for medical students written by an Indian author and the appearance of the 15th edition bears silent testimony to its usefulness and wide popularity. During the last two decades, of all the subjects in the pre-medical curriculum, the teaching of materia medica has perhaps undergone the most radical changes. Instead of asking the student to master the old-fashioned materia medica with all its uninteresting and perhaps useless details of the origin, source, collection, method of preparation and doses of drugs, emphasis is now rightly laid on

the nature and mode of action of drugs on the biological tissues and human systems. This has necessitated a thorough reorientation of teaching and with it, a demand for textbooks reflecting this new method of approach to the subject-matter. It is no mean credit to the present author that he has succeeded in bringing about a happy blending of all that is acceptable in the older and newer concepts and in presenting a textbook that caters admirably for the demands of the modern student. This would have wellnigh been impossible for anybody without a sound knowledge of, and familiarity with, the essential needs of the students.

The present edition embodies all the new additions mentioned in the *Addendum* to the B. P. (1936) and a number of other significant therapeutic advances such as sulphanilamide, mandelic acid, nicotinic acid, etc. There is also evidence of thorough textual revision to bring the subject-matter abreast of modern times. The introduction of empirical and constitutional formulae of many organic and synthetic remedies is an innovation in this edition which should be welcome. In line with the modern concept of teaching scientific pharmacology, the author has included 29 illustrations in apposite places in the text depicting the action of various drugs on the different systems of the body. The grouping and the description of individual drugs under various sub-headings are generally satisfactory. In the section dealing with applied pharmacology and therapeutics, the treatments suggested are mostly conservative and represent accepted opinion. Data judged to be still in the experimental stage are generally avoided.

While the text throughout is written in clear, lucid style and every portion of the book is readable, the student, for whom the treatise is primarily meant, is apt to object that he is being offered too much material, touching on all aspects of pharmacology, materia medica including Indian indigenous drugs, toxicology, therapeutics and pharmacy, which he would find it difficult to digest. Without detracting from the usefulness of a knowledge of pharmaceutical processes in the medical curriculum, it is questionable whether the introduction of so much pharmacy in a textbook of this nature and scope is really desirable. Objection may also be raised to the rather extensive use of small type which the reviewer is inclined to think is likely to be a little tiring to the eyes of the readers. This is understandable when it is confined to the treatment of matters that are at present largely controversial or to descriptions of non-official preparations or data of comparatively minor interest to students, but when this is extended to the introductory remarks to the various chapters and sub-sections dealing sometimes with the fundamental principles of drug action, one is inclined to think that the author's idea of condensation and economy of space has been carried a little too far. A volume containing the same amount of reading matter printed in Great Britain or America for instance, would easily have occupied one and a half times the space covered by this volume.

The first section of the chapter on chemotherapy is a little disappointing. Instead of giving the student a conventional definition of the term and a general description of the evolution and scope of chemotherapy, which is to be legitimately expected, the author has given a very good and illuminating note on the physio-pathology of the reticulo-endothelial system which, though useful to the practitioners, may be a little too high standard for the average students. A few blemishes and printer's errors have also crept in. As instances to the point may be mentioned the spelling of 'venyl ether' and of 'cyclopropaine'. On page 292, in the constitutional formulae of adrenaline and ephedrine, the carbon atom shown at the point of introduction of the side-chain is redundant. References to the literature cited in the text and in the footnotes have been given haphazard (*cf.* p. 450) and full details regarding year, page number, etc., of the journals mentioned are lacking.

These blemishes which can be easily rectified in a subsequent edition are only minor and do not detract

from the usefulness of the book which may justly be placed in the very front ranks of similar textbooks in the English language.

B. M.

**AN OUTLINE OF MEDICAL PSYCHOLOGY.**—By E. Fretson Skinner, M.A., M.D., F.R.C.P. 1939. H. K. Lewis and Company, Limited, London. Pp. viii plus 173. Price, 6s.

THE author states that this little book represents an attempt to place before the non-technical reader and medical students entering on their professional curriculum some of the facts and hypotheses of modern psychology, as applied to the causation of nervous diseases, and their treatment by its means. No doubt this rather turgid sentence describes more or less exactly the purport of the book. At the same time, the condensation of the subject-matter is so intense as to render its exposition somewhat difficult to follow. Nevertheless, for a lay reader at any rate, the book contains a good deal which will repay perusal. The author is an exponent of psycho-analytical therapy and has not much to say about any other psycho-therapy. As regards the attitude of the law towards homosexuality in adults, the author is correct in stating that the law only seeks to punish homosexuality among men and not among women, but he omits to observe that this is British law. In some countries, e.g., Italy, the law does not take cognizance of homosexuality and in others, e.g., Sweden, both men and women are liable to punishment for practising homosexuality. The book concludes with a presentation of a few clinical histories. For some unexplained reason, the author regards sexual fetichism as a form of obsessional neurosis. This

appears to connote a lack of understanding on the part of the author of the ætiology of the two conditions.

O. B-H.

**THE SANITARY INSPECTOR'S HANDBOOK. A MANUAL FOR SANITARY INSPECTORS AND OTHER PUBLIC HEALTH OFFICERS.**—By H. H. Clay, F.R.San.I., F.I.S.E. Fourth Edition. 1939. H. K. Lewis and Company, Limited, London. Pp. xxii plus 528, with 97 illustrations. Price, 17s. 6d.

BOTH the book and its author are too well known to need introduction. The book has been recognized as a standard textbook on sanitary inspection, particularly for students preparing for London examinations. It should be a standard reference work for practising sanitary inspectors and public health administrators. The fact that the book has reached its fourth edition in so short a time is evidence of its growing popularity and usefulness.

The present volume, which retains the commendable qualities of the previous editions, contains much new matter and some new illustrations, the principal change being the chapters on food and food premises which have been re-written.

The book is written for English conditions that are largely urbanized and consequently has very obvious limitations for India. The latter are particularly in the fields of rural sanitation in general and malaria in particular.

The usefulness of the book is greatly enhanced by the excellent index and by its glossary of terms and appendix of comparative tables and definitions.

## Abstracts from Reports

### ANNUAL PUBLIC HEALTH REPORT OF THE PROVINCE OF ASSAM FOR THE YEAR 1937. BY LIEUT.-COLONEL A. M. V. HESTERLOW, M.B., Ch.B. (EDIN.), B.Sc., P.H. (EDIN.), D.T.M. & H. (EDIN.), I.M.S., DIRECTOR OF PUBLIC HEALTH

**Kala-azar.**—The number of deaths from kala-azar during the year 1937 was larger by 304 than that of 1936. The number of patients treated was also larger by 1,464. The increase both of deaths and cases treated is shared by Sylhet, Goalpara, Nowgong and Sibsagar districts. The method of diagnosis and treatment of kala-azar continued to be the same as in previous years. Special attention continues to be given to intensive and detailed surveys in all districts in order to detect fresh cases and bring them under treatment as early as possible. A sub-assistant surgeon was deputed to Cachar district specially for kala-azar survey duty. The sub-assistant surgeons in charge of hospitals and dispensaries also surveyed 514 villages during 1937.

**Cholera.**—The number of deaths from cholera during the last 10 years was as follows:—

1927	..	..	..	15,392
1928	..	..	..	6,915
1929	..	..	..	7,765
1930	..	..	..	6,332
1931	..	..	..	5,523
1932	..	..	..	4,971
1933	..	..	..	5,508
1934	..	..	..	1,904
1935	..	..	..	7,436
1936	..	..	..	3,816
1937	..	..	..	5,440

The increase of cholera mortality in 1937 was due to an increase of the disease in the district of Sylhet. In this district 4,371 persons died from cholera against

2,047 in the preceding year. At first the outbreak was of a sporadic nature but later it assumed an epidemic form owing to the scarcity of drinking water. Delay in reporting the outbreaks also helped in permitting the outbreak to become widespread. In other districts only sporadic cases occurred.

#### RURAL SANITATION

About 97 per cent of the population of Assam live in rural areas, consequently the health and prosperity of the people of these areas is a matter of vital importance. Local boards should pay special attention to the provision of adequate and safe water supplies for villages. Until this is done no material reduction in the incidence of water-borne disease can be expected. The public health measures which are extensively carried out in rural areas are protection against cholera by inoculation, the use of bacteriophage in the treatment of cholera cases and protection against smallpox by vaccination. Kala-azar treatment measures continue to be carried out on the lines similar to those employed hitherto. Tablets of quinine-reinforced cinchona febrifuge for the treatment of malaria are sold in all village post offices and through other accredited agents. Quinine and cinchona febrifuge are also supplied free to indigent persons in all districts. Treatment of yaws, leprosy, malaria, influenza, minor eye complaints, dysentery and diarrhoea is also undertaken by public health department dispensaries in the rural areas. Adulteration of foodstuffs is reported to be increasing in the Province. This may be controlled by more strict supervision, by regular inspection and submission of samples to the public analyst for analysis, and inflicting of adequate punishment in all cases where food unfit for consumption is sold, and where adulteration of articles of food is reported by the analyst. It is hoped that local boards will take more active and deterrent action to prevent adulteration than appears to be the case at present.



**Malaria.**—Malaria fever is the most widespread disease in the Province. It is prevalent throughout the Province and almost constantly in epidemic form. A total of 819,845 cases of malaria were treated in all hospitals and dispensaries in the plains districts; 716,192 cases were treated in dispensaries under the medical department and 103,653 cases in the public health department dispensaries. Separate figures of mortality from malaria are not available. As noted in paragraph 25, deaths from 'Fevvers' amounted to 109,375 against 97,240 in the preceding year. A very large percentage of these deaths must be attributable to malaria fever. Quinine-reinforced cinchona febrifuge was used as a general preventive and curative agent against the disease and was sold to the public at two annas per tube containing ten tablets of four grains each. As in previous years the Government of Assam gave a grant of Rs. 20,000 to Assam Medical Research Society. The Society's activities are at present confined mainly to researches on malaria.

**Maternity and child welfare.**—During the year under report the Juarmal Tusnial Maternity and Child Welfare Centre with hostel for accommodation of 12 women for the *dai* training class was opened at Syllhet. Maternity wards were opened at Sunamganj and Maulvibazar during the year. A maternity ward with 14 beds, operation room and sanitary annexe, etc., are also under construction at Karimganj.

A total of 39,727 infants died during 1937 giving an infant mortality rate of 160.04. This large number of deaths amounting to nearly 109 infants per day can be reduced if more maternity and child welfare centres are opened throughout the Province and a larger number of properly trained midwives is made available. The maternity and infant mortality rates recorded in rural areas were 15.13 and 161.13 and those in urban areas were 19.34 and 120.95 respectively. The maternal mortality for the whole province is 15.24. The number of deaths from child birth is collected through Chaukidars and Gaonburas. Beyond the usual verification of vital statistics no special enquiries have been made to verify and check these statistics. The death rate of children under 5 years was 71.95. The high infant mortality rate is due to lack of knowledge regarding maternity and child welfare. The child welfare and maternity organization is in the hands of the Red Cross Society. No portion of the public health department's budget was allocated to maternity and child welfare. There was no specialized work for women and children in industrial areas. The number of beds during the year was 47.

#### ANNUAL REPORT OF THE HENRY LESTER INSTITUTE OF MEDICAL RESEARCH, SHANGHAI, FOR 1937-1938

This report differs from its predecessors in that it covers a period of two years, 1937 and 1938. During the first six months of 1937 work proceeded normally except for the welcome interruption of the medical conferences held during April. These attracted a record attendance and marked the opening of the new Hospital and Buildings of the National Medical College of Shanghai. From August 1937 to September 1938 the Institute, in company with other organizations in Shanghai, had to adjust itself to new conditions and during this period the main building was closed, except for the period from August to January when it was used by the General Hospital. Most of the foreign staff were sent to England on leave and those about to return were told to remain in England. It was decided, however, that every effort should be made to maintain the integrity in the Institute as a working organization by means of a skeleton staff and this was made possible through the suspension of clinical research and the use of the Clinical Unit, laboratories for general purposes. Gratitude must also be expressed for academic hospitality, to the Shanghai Municipal Council, the University of Hongkong, the King Edward VII Medical College, Singapore, and the London School of Hygiene and Tropical Medicine.

[In spite of the restrictions indicated in the above paragraph a large amount of research work appears to have been carried out. It is of too detailed a nature to lend itself to abstraction but the report contains much interesting matter particularly on nutritional problems and nutritional diseases in China.—EDITOR, I. M. G.]

#### ANNUAL REPORT OF THE MYSORE STATE DEPARTMENT OF PUBLIC HEALTH FOR 1937

**State of public health.**—Except for an increase in the incidence of plague and cholera and a decided decrease in the incidence of smallpox, the general state of public health, as indicated by the mortality and morbidity rates, was normal.

Cholera assumed epidemic proportions in Mysore, Shimoga and Chitaldrug districts, the number of deaths reported from the disease being 4,239 as against 1,793 in 1936. Three lacs, eighty-two thousand, two hundred and thirty-nine anti-cholera inoculations were done during the year, of which 159,644 were done in the Mysore district alone. In the city of Mysore, there were 341 attacks and 177 deaths and the number of inoculations performed was 67,349, while in the city of Bangalore, the number of attacks, deaths and inoculations was 55, 29 and 4,596 respectively.

A preliminary study of statistics of cholera in the state from the year 1887 was made and the following were the conclusions reached:—

- (i) The state is not highly infected with cholera, but some districts are open to periodic outbreaks especially in, what may be called, epidemic years;
- (ii) there are two gateways by which infection is brought into the state, viz,
  - (a) along the Yelandur-T-Narsipur border and
  - (b) along the Harihar-Davangere border;
- (iii) although the state as a whole is not highly infected, a few *taluks* at least, and some smaller foci show continued infection.

Plague was reported chiefly from Bangalore, Kolar and Hassan districts, the number of deaths from the disease being 4,842 (1,793). The number of anti-plague inoculations done was 221,080.

Deaths from smallpox were 1,095 (4,973). The number of vaccinations performed was 247,784.

Deaths from typhoid were slightly more this year, both in the Mysore and Bangalore cities, the number being 63 (51) in the Mysore city and 88 (61) in the Bangalore city. A number of anti-typhoid inoculations were no doubt performed, but there is need for further systematic investigation into the causes of this disease and for taking effective measures to prevent its recurrence.

**Vital statistics.**—In pursuance of the recommendations of the Committee on Vital Statistics, the revised system of registration and compilation of the statistics of births, deaths and marriages was introduced into the Bangalore and Mysore cities and the Kolar Gold Fields and into the districts of Bangalore and Shimoga.

The total number of births during the year was 146,737 (136,569). The computed birth rate was 21.6 as compared with 20.3 in the previous year. The highest birth rate was reported by the Chitaldrug district (24.5) and the lowest by the Kadur district (15.4).

The total number of deaths during the year was 102,118 (96,278). The computed death rate was 15.1 per mille of population. Births exceeded deaths in all districts except Shimoga. The total number of deaths among children under one year of age was 15,567 (15,895), giving an infant mortality rate of 106.1 per 1,000 live births against 116.6 in the previous year. The total number of deaths due to child birth was 2,191 (2,128), the mortality rate being 14.7 (15.3) per 1,000 births.

**Public health institute.**—A new section was started in the institute during the year for the manufacture of plague vaccine, in addition to the preparation of

T.A.B. and anti-cholera vaccines. Experimental work was also continued in connection with the standards of purity of articles of food as well as the nutritional value of rice, ragi, etc.

**Bureau of health education.**—Two health exhibitions were held at Mysore, one in connection with the Dasara exhibition and the other in connection with the annual Swadeshi exhibition. A health museum has also been established in Mysore city as a permanent feature in the new exhibition buildings.

**Bureau of rural health.**—The health training centre at Closepet continued to do good work. Health leagues were started in 16 villages in the area, with the following programme:—

- (1) Providing latrines of standard type to individual houses;
- (2) introduction of windows;
- (3) white-washing;
- (4) improvement of flooring;
- (5) removal of manure pits from the village site;
- (6) improvement of water-supply, and
- (7) improving the cleanliness of the village generally.

In the rural health unit, Mandya, no marked change was visible in the incidence of malaria. The control of malaria in Mandya town was continued under the supervision of the unit staff.

**Bureau of epidemiology.**—The work of the bureau consists of organizing measures for the control of epidemic diseases including malaria and conducting the campaign against hookworm and guinea-worm.

The annual spleen and parasite survey of Bangalore city was done as usual. The spleen rate for the whole city was found to be 0.31 (0.30) and the parasite rate 0.5 (0.8). In Mysore city, a combined programme for the control of general mosquito nuisance in certain sections of the city and selective anopheline control as a purely anti-malarial measure in the other sections was carried out during the year. Malariol was used for controlling mosquito nuisance and Paris green for anopheline control. The spleen and parasite rates in the three malaria stations during the year were as noted below:—

Station	Spleen rate		Parasite rate	
	1937	1936	1937	1936
Nagenhalli ..	22.1	24.1	5.8	6.5
Hriyur ..	45.6	26.4	12.0	7.9
Mudgere ..	28.2	23.1	2.8	2.2

A new type of latrine for rural areas, which is very promising as a means of eliminating fly breeding, was evolved and was under trial in Chikballapur. The hookworm staff visited 26 villages in the Periyapatna sub-taluk and treated 2,367 persons. They also visited 136 villages in the Krishnarajpete taluk and treated 9,592 persons out of a total population of 47,032. Three hundred and fifty-eight public latrines of the 'hagevu' type were constructed in 50 villages.

The guinea-worm staff visited 832 villages, examined 440 wells, chlorinated 55 wells, restocked 97 wells with fish and newly stocked fish in 70 wells and established 32 nurseries. Since 1928, 122 well works have been undertaken as a means of controlling guinea-worm disease at a cost of Rs. 1,16,434.

**Important measures.**—Among the important events of the year may be mentioned—(1) the transfer of the regulation of maternity and child welfare work from the health to the medical department; (2) placing the services of a medical officer at the disposal of the Red Cross Society for appointment as secretary; (3) training 21 students in the sanitary inspectors' training class; and (4) the appointment of two public health probationers.

BLINDNESS IN INDIA. PUBLISHED BY THE NATIONAL INSTITUTE FOR THE BLIND, 224-6-8, GREAT PORTLAND STREET, LONDON, W.1.

THE census of 1931 gave the number of blind persons in India and Burma as 601,370, or 172 per hundred thousand of the population. Census returns generally tend to under-statement of physical defect, and this tendency to under-statement is probably specially strong in India, where purdah influences would be opposed to the notification of blindness in girls of marriageable age. Sir John Megaw states that from random samples of villages investigated in a survey made by him a few years ago, it would appear that there are about two million blind people in India.

The late Mr. C. G. Henderson, founder of the All-India Blind Relief Association, in an address delivered at the World Conference on Work for the Blind, held in New York in 1931, spoke as follows:—

'It is estimated that there are one and a half million totally blind persons, and in addition, some four and a half million persons partially blind. . . . In 1918, in the district in which I was serving, I had a list of blind and partially blind persons made out in an area containing about 250,000 population, and then inspected the totally blind. I found at least four and half per thousand. The same thing was done in several districts, with the results that we found that three, four, seven, and even nine per thousand of the population were totally blind, as against the census average of one and a half.'

The estimate given by Mr. Henderson in this extract is rather more pessimistic than that given by the Indian Red Cross Society. 'There are in India, about one million blind persons, and for each blind person there are three others with seriously impaired sight'.

#### *Prevention of blindness in India*

The problem of prevention of blindness is a most pressing one. Although no exact figures are available as to causation, it is indisputable that a great part of India's blindness is due to infantile ophthalmia, to neglect of simple eye diseases in children, to the application of irritant remedies, to smallpox and to trachoma, all of which are preventable, or can be remedied by proper treatment.

Although with the death of Mr. C. G. Henderson in 1931 the activities of the Association which he had founded came to an end, the work which he did for prevention of blindness in India indicates the line of attack which will probably be followed in the future, and which characterizes the work of such organizations as the Bengal Association for the Prevention of Blindness. The problem of blindness, like so many others in India, is one peculiarly affecting the rural population. 'The towns of India only account for a small part of its three hundred and fifty million inhabitants, most of whom can only be reached if help is brought directly to them.' The special merit of Mr. Henderson's gallant enterprise was its recognition of this principle. The fourfold basis of his campaign was outlined by him as follows:—

1. Prevention, by means of personal effort in the visitation of the villages, with special reference to treatment of ophthalmia neonatorum and the vaccination of all smallpox contacts.

2. Propaganda, by means of pamphlets printed in the vernaculars, lectures by touring medical officers, films showing dangers of infection, and co-operation with village officials in matters relating to eye diseases and sanitation.

3. Sight-saving in schools, with inspection of the children and treatment where necessary, together with talks to the children on matters concerning the care of the eyes.

4. Establishment of touring hospitals. The touring eye surgeon to camp at certain central villages, where sufferers from eye diseases from the surrounding country can come to him for treatment or operation.

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These recommendations were in many respects similar to those passed at a Conference of the All-India Ophthalmological Society in 1935.

#### *Education in India*

The inquiries made in 1930 showed that although there were rather more than twenty schools for the blind in India, the majority of these were small, probably not accommodating more than about a dozen pupils. Only the most elementary curriculum of reading, writing and arithmetic was attempted, together with a little handwork, and few children remained at school long enough to derive real benefit. The fact that there was no system by which the child could pass from school to training-centre, and from training-centre to workshop, made a dead-end of education in many of the schools, and parents were disinclined to allow their children to attend. Begging is the recognized and time-honoured form of livelihood for the blind in India, and it must be admitted that there is little encouragement for those who desire something better.

#### *Industrial training*

There is very limited provision made in India for the industrial training of the blind, partly because few pupils remain long enough at an institution to avail themselves of it, and also because the training-centre is only one stage of any properly conceived plan for the blind, and workshops where trades can be carried on by the trained worker are a necessary corollary.

#### *Memorial of the Secretary of State*

A conference was held, of persons with knowledge of India or special experience of work for the blind in this country, and it was decided by them that the problem was altogether too vast for private enterprise to attempt a solution. In March 1931, a Memorial was addressed to the Secretary of State for India, concentrating especially upon the known facts of preventable blindness in India, and expressing the hope that some action might be taken by the Government. The signatories to the Memorial included a former Viceroy, two former Governors of Indian provinces, two former Indian bishops, a former Educational Commissioner with the Government of India, and several medical men with experience of ophthalmological work in India.

The Memorial was referred by the Secretary of State of Local Governments and Administrations for their consideration, and at a later date a further letter from the National Institute to the Secretary of State was also referred to these bodies. In this letter the hope was expressed that an advisory committee might be set up in India, consisting of persons actively engaged in work for the blind, which would bring together the knowledge and experience of existing organizations for the welfare of the blind and the prevention of blindness.

It was with great regret that the National Institute learned from the Secretary of State for India in June 1933 that almost all Local Governments had expressed their inability, owing to financial stringency, to incur expenditure on the development of measures for the prevention of blindness or for the provision of relief for the blind, and that the majority of them were not in favour of the proposal for the formation of an advisory committee.

#### *Co-operation with the Indian Red Cross Society*

The hope of Government action having been thus for the time disappointed, the committee met once more, and decided in November 1932 that its best hope of effective action lay in co-operation with the Indian Red Cross.

In April 1934, the National Institute for the Blind made a grant of £570 to the Indian Red Cross Society, of which £450 was allocated for the systematic instruction of teachers in blindness prevention, and £120 for the provision of simple pamphlets on prevention in Bengali, Tamil and Telugu. At a later date, through

the kindness of a private donor, a further sum of £30 was granted to finance Hindi and Urdu editions of the pamphlets.

In February 1936, the Junior Red Cross issued a most interesting report on the expenditure of the grant. Four of the leading ophthalmologists in India had been consulted regarding the organization of the lectures for teachers, and a syllabus had been drawn up for a course of two lectures, followed by practical demonstrations. Each lecturer was supplied with a set of coloured slides, and with a list of all material—pamphlets, posters, slides and films—on prevention of blindness, obtainable from the Red Cross Society.

A circular letter was then sent out to all Provincial and State Red Cross branches, inviting them to carry out the scheme through the agency of the Junior Red Cross, which has 10,000 school groups, and a membership of 350,000 school children. Reports were received in due course from eighteen of these.

The National Health Association of Southern India has also been active in arranging lectures for school teachers, held at the Teachers' College, Saidapet, and elsewhere, with a view to educating the teachers in the principles of blindness prevention.

In May 1936, the National Institute for the Blind made a further grant of £170 to the Indian Red Cross, for the provision of pamphlets in Canarese, Marathi and Sindhi. As a result, 30,000 pamphlets were published during the year in these languages, and also in Bengali and Hindi, and distributed through the Directors of Public Health and Public Instruction, as well as through the Indian Red Cross Society.

In December 1937 a letter was received from the Red Cross Society, giving a report on the work of the Junior Branch in connection with prevention during the year. Since that date, a further report has been received, and a further grant made by the National Institute, for the organization of more lectures, free lantern slides and posters, and the provision of more vernacular literature.

For the large number of persons who are illiterate, and for whom pamphlets are therefore unavailing, reliance is placed on films and broadcasting.

The Association for Prevention of Blindness, Bengal, has set a valuable example of the way in which blindness may be combated, 'by bringing the benefits of modern ophthalmology to the very doors of the people in the remote villages'.

A gift of Rs. 35,000 was made to the Bengal Association by the committee responsible for the administration of the fund raised to commemorate the Silver Jubilee of Their Majesties King George V and Queen.

The first stage of future action must be to stop the flow of recruits to the army of the Indian blind. Valuable preventive work has been done by the All-India Blind Relief Association, the All-India Ophthalmological Society, the Bengal Association for the Prevention of Blindness and the Indian Red Cross Society, all of which organizations are at one in emphasizing the importance of propaganda by lectures, pamphlets, broadcasts, posters and films, and of the value of bringing preventive measures into the homes of the people by means of travelling hospitals, camps and dispensaries. In a small way, and crippled by small resources, these organizations have indicated what might be done on a far wider scale with adequate financial backing.

[This pamphlet is a valuable contribution to one of India's principal public health problems and it should be circulated as widely as possible throughout the country.—EDITOR, I. M. G.]

#### ANNUAL REPORT OF THE MALARIA ADVISORY BOARD, FEDERATED MALAY STATES, FOR THE YEAR 1935

THIS is always an interesting and valuable publication, but as it contains only condensed summaries of the various anti-malarial activities carried out under the direction of the Board it does not lend itself to further abstraction. Practically all methods of

mosquito control and malarial treatment and prophylaxis are practised in one or other locality in the Federated Malay States so it is a complete and concise résumé of modern anti-malarial measures in general. All medical officers whose duties are concerned with this subject, especially those working anywhere in India or east of it, should obtain a copy of this report, because they cannot fail to find something in it that will have a bearing on their special local problems whatever they may be.

#### ADMINISTRATION REPORT OF THE BALUCHISTAN AGENCY FOR THE YEAR 1ST APRIL, 1937 TO THE 31ST MARCH, 1938

The principal diseases for which treatment was sought during the year and their geographical distribution are shown below:—

in the laboratory. None was found infected. The flea index remained low, being only 1.07 per live rat against 1.81 in the previous year.

#### ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH: ANNUAL REPORT BY THE CURATOR OF THE LABORATORY FOR THE YEAR 1938

##### STATISTICS OF ANTI-RABIES TREATMENT

The eighth analytical review of the results of anti-rabies treatment at the Pasteur Institutes of the world which submit statistics to the League of Nations, prepared by the superintendent, has now been published. It is noteworthy that the main conclusion therein arrived at—that as an immunizing agent killed carbolized vaccine when given in suitable dosage is as

Name of disease	Quetta-Pishin District	Sibi District	Loralai District	Zhob District	Kalat and Chagai Districts	Total
Malaria—						
Treated .. .. .	25,137	27,812	17,226	15,028	28,001	113,204
Deaths .. .. .	5	1	1	..	1	8
Dysentery—						
Treated .. .. .	1,130	320	160	76	806	2,492
Deaths .. .. .	2	..	1	1	..	4
Diarrhoea—						
Treated .. .. .	2,621	2,108	876	948	2,687	9,240
Deaths .. .. .	1	2	..	..	..	3
Ulcerative inflammation—						
Treated .. .. .	16,330	16,036	15,476	9,464	16,175	73,481
Deaths .. .. .	1	..	..	..	..	1
Rheumatic fever—						
Treated .. .. .	145	230	14	61	107	557
Deaths .. .. .	..	..	..	..	..	..
Diseases of respiratory system other than pneumonia and tuberculosis—						
Treated .. .. .	10,184	11,071	7,210	5,741	17,057	51,263
Deaths .. .. .	4	..	1	..	..	5
Other diseases of the digestive system excluding diarrhoea, dysentery and tumours—						
Treated .. .. .	24,441	22,584	15,447	11,913	28,334	102,719
Deaths .. .. .	1	1	..	..	1	3

#### ANNUAL REPORT OF THE HEALTH DEPARTMENT, MUNICIPALITY OF SINGAPORE, FOR THE YEAR 1938

APART from two cases of smallpox we enjoyed another year of complete freedom from the three dangerous infectious diseases, smallpox, cholera and plague. Even with one of the smallpox cases there was an element of doubt in the diagnosis. It came from a house in which there were at the same time several cases of chickenpox. The other was a frank case of smallpox. At first he gave a history of having just arrived from India but later denied this. As no connection with any previous case could be found and no further cases developed in the contacts, the likelihood is that the first story was the correct one and that he was discovered within a very short time of his arrival in the colony.

In connection with plague the usual rat-trapping laid down by the International Sanitary Convention was carried on throughout the year. Four thousand and five rats trapped in the town and port area were examined

efficacious as living vaccine, whilst at the same time it reduces the risk of accident to a minimum—has now been accepted by the French School. In fact, Remlinger, the leader of that school, now strongly advocates the general adoption of this method of treatment. This view was put forward by the superintendent at the Rabies Conference in Paris in 1927, and it is satisfactory that in the light of further statistical data it has now been accepted.

A ninth review is now in preparation. It will deal with statistics relating to the years 1936 and 1937. As a measure of retrenchment it has been decided by the League of Nations that future reviews will deal with the statistics of two successive years, and will be published every alternate year. The data to be dealt with relate to approximately 200,000 treated persons.

*Parasitology.*—*Trichomonas vaginalis* has been found to be present in the vagina of approximately one-half of 200 consecutive female patients who were examined and who were attending a venereal diseases clinic in Edinburgh. The presence of the parasite was detected in 45 per cent of 100 pregnant women suffering from



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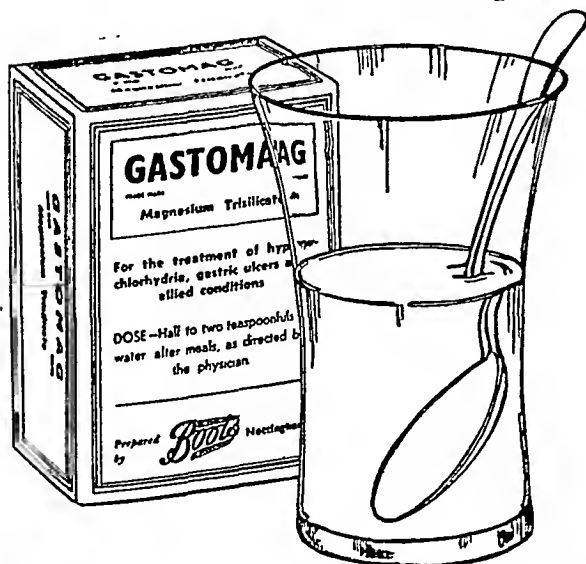
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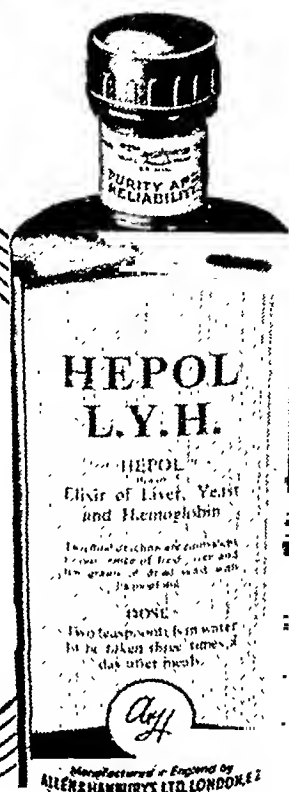
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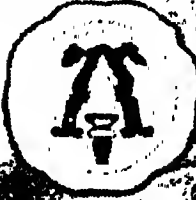
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a discharge and attending the ante-natal clinic of the Maternity Hospital. There is no doubt therefore that *T. vaginalis* is common in this class of patient. It is little doubt that the presence of the parasite in the vagina is a definite cause of leucorrhœa. The disease is frequently mistaken for gonorrhœa and thus gives rise to awkward social problems. The confusion between the two infections of entirely different ætiology is the more likely to occur because it has been found that in as many as 50 per cent of women suffering from gonorrhœa, the presence of *T. vaginalis* complicates the disease. The importance of this fact is evident since it is known that the administration of the drug M. & B. 693 rapidly causes the disappearance of gonococci from the vagina, although the drug has little, if any, effect upon *T. vaginalis*. Cases of gonorrhœa complicated with a trichomonas infection are not cured by the administration of M. & B. 693; the leucorrhœa continues in spite of the administration of the drug.

The type of leucorrhœa caused by *T. vaginalis* presents certain characteristic signs and symptoms, particularly during the acute phase of the disease. A latent form of the infection has been observed which can assume an acute phase when from any cause the hydrogen-ion concentration of the secretion of the adult vagina becomes altered. The mechanism which maintains the hydrogen-ion concentration of the vaginal secretion of the adult female at a pH of between 4 or 5, and thus eliminates infection by *T. vaginalis*, is now being studied. *T. vaginalis* does not multiply in such an acid secretion.

A number of males infected with *T. vaginalis* have been found, and the prevalence of this infection among men attending one of the venereal diseases clinics in Edinburgh is under investigation. The possibility that men can be infected with *T. vaginalis* has shed some light on so-called cases of 'non-specific urethritis'.

#### ANNUAL REPORT OF THE NATIONAL ASSOCIATION FOR SUPPLYING MEDICAL AID BY WOMEN TO THE WOMEN OF INDIA (COUNTRESS OF DUFFERIN'S FUND INCLUDING THE WOMEN'S MEDICAL SERVICE) FOR THE YEAR 1938

The first All-India Conference of Medical Women was held in Delhi under the Patronage of Her Excellency the Marchioness of Linlithgow from 13th to 15th December, 1938. The Conference was opened by Sir Ernest Burdon, K.C.I.E., C.S.I., I.C.S., and the deliberations were presided over by Dr. Dadabhoi, President of the Association of Medical Women in India. Eighty-three delegates attended the conference from all parts of India. The discussions on 'Eclampsia' and 'Anæmias in Pregnancy' brought out more strongly than ever the important part these diseases play in causing the high maternal mortality which prevails throughout India. The great need there is in this country for up-to-date midwifery services, more and better equipped hospitals for women and travelling dispensaries was stressed by every speaker. It is the right of every woman to be able to claim adequate attention before, during and after child birth.

A recent tour undertaken by the Secretary in the North-West Frontier Province at the request of the Inspector-General of Civil Hospitals and with the concurrence of the Provincial Government, it showed the women of the N.-W. F. Province are becoming hospital-minded and are seeking admission to hospitals for women in ever increasing numbers. Especially is this so in the case of maternity patients whose numbers have more than doubled during the last few years. The hospital accommodation is now totally inadequate to meet the demand and the existing hospitals for women are all overcrowded and understaffed. A similar state of affairs exists practically throughout India. It seems 'purdah' is rapidly breaking down, but there are still a large number of women who would die rather than enter a general hospital and a still larger number

who would prefer to be attended by a member of their own sex for their confinements and for special diseases of women.

There is thus a very strong case for enlarging hospitals for women and for building new ones. Equipment should be modernized and the medical and nursing staffs should be brought more nearly up to the standards existing in Europe and America. The local authorities seem to be unable to give proper financial support to the hospitals under their administration and evidence is accumulating supporting the recommendations made by various experts that the control of the majority of these hospitals should be handed over to the respective provincial governments. This procedure, if carried out, should lead to an all-round improvement, as, presumably, the financial support given by the local governments would be more in keeping with the requirements of the institutions.

The urgent need for increased medical aid in the rural areas is being more and more stressed on every hand and it is satisfactory to note a scheme for an ambulance service has been inaugurated in the United Provinces.

The recurring income of the Countess of Dufferin's Fund amounting to approximately Rs. 40,000 has been spent during 1938, in grants to Provincial Dufferin Branches and to various hospitals. A sum of Rs. 9,080 was spent on 24 scholarships to students in medical colleges, 14 are awarded from Association funds and the remainder from trust funds administered by the Dufferin Council.

The imperative need for more money for the upkeep of the Dufferin Hospitals was stressed in the report for 1937; inspection of these hospitals in 1938 only reveals more clearly how pressing this need is and the Secretary in her inspection reports has reiterated the urgent necessity there is for repairs and additions to the hospitals. The supply of equipment and nursing staff is still most inadequate.

A comparative study of the annual statistics of the 25 hospitals in charge of W. M. S. officers shows the remarkable increase there has been in the number of admissions to these hospitals during the period 1929 to 1937.

TABLE

Year	Number of in-patients	Number of obstetric cases	Number of operations performed
1929	.. 0,509	7,263	17,686
1933	.. 43,020	10,358	19,758
1935	.. 51,853	13,606	22,630
1937	.. 52,902	16,219	24,591

The number of out-patients treated has also increased during the same period from 794,565 in 1929 to 980,874 in 1937.

The statistics given above are sufficient evidence to prove that our Dufferin Hospitals are not suffering from 'unpopularity', in spite of insufficient accommodation, staff and equipment.

Unfortunately the accommodation in 1939 is only slightly greater than that available in 1929, so that the problem of overcrowding in all the hospitals is a very serious one.

The new Dufferin Hospital for Women and Children, Calcutta, is nearing completion. It is a modern 3-storeyed building with accommodation for 200 patients. The planning has been carried out with great care not only to provide the best accommodation possible for the patients but with an eye to economy in space and in administration. A grant of Rs. 1,75,000 was given from the Silver Jubilee Fund towards the re-building of this hospital. Funds are still to be raised for a nurses' home, servants' quarters, hospital kitchen and a laundry.

It is very satisfactory to record that the Dufferin authorities at Amraoti have at long last realized their

dream of building a new hospital. It is hoped that it will be completed shortly. At present the new buildings will only accommodate 50 patients, but the site is such a spacious one, there is ample space for expansion in the future. The nurses' home is an excellent building and has been planned with care and forethought for the comfort of the nursing staff. A building grant of Rs. 30,000 was sanctioned from the Silver Jubilee Fund.

## ANNUAL REPORT OF THE PUBLIC HEALTH COMMISSIONER WITH THE GOVERNMENT OF INDIA FOR 1937. VOLUME II

### PRINCIPAL DISEASES AFFECTING THE BRITISH ARMY. HEALTH OF THE ARMY IN INDIA DURING 1937

1937 has been, from the health aspect, a good year for both British and Indian troops. There was a reduction in hospital admissions among both groups as compared with 1936 (also a good year), of 14.3 per 1,000 of strength among British troops, and 37.0 per 1,000 of strength among Indian troops. The admission ratio appears generally to be on the downward trend and although an improvement on that of previous decades (in 1920 it was 1,071.5 per 1,000 for British troops and 762.3 per 1,000 among Indian troops), cannot be considered satisfactory according to modern health standards as long as approximately 568 out of every 1,000 British soldiers and 390 out of every 1,000 Indian soldiers are admitted to hospital during the course of a year. When compared with the admission ratio to hospital among the troops in the United Kingdom the ratio in India is found to be almost exactly double. The reasons are partially climatic, and partially the more primitive methods of sanitation, particularly with regard to conservancy, available not only for the army, but also for the civil populations in contact with them. Education, finance and time are the three main factors concerned given the will gradually to progress up to modern standards. It is satisfactory to record in addition to the drop in hospital admissions a reduction in the average constantly sick, death and invaliding rates.

An encouraging feature during the past few years and particularly during 1936 has been the reduction in incidence of such diseases as malaria and the enteric group of fevers.

#### Malaria

The malaria incidence during 1937 is the lowest yet recorded for the British troops in India and nearly one-third less than in 1933. The ratio per 1,000 would have been even lower had it not been for an increase of 20 per 1,000 in Western Command. It was estimated that at least 50 per cent of the cases among the Quetta garrison were contracted during the training season, nets not having been used. The incidence in this station rose from 113 (1936) to 194 per 1,000 in 1937.

The low incidence of malaria for all-India was undoubtedly helped by favourable weather conditions, particularly in the north. In that area August was an unusually dry month, and in July and October there was rather less rain than usual. Cold weather also set in earlier in the autumn than is customary. In the Eastern Command, the monsoon was late, deficient in certain areas and patchy in others.

The ratio per 1,000 of relapses for all-India is also just less than half of that in 1933, and there is little doubt that this is mainly due to the plasmoquine now invariably combined with quinine or given after the atebirin course of treatment.

Treatment was carried out sometimes with quinine and plasmoquine but mainly now with atebirin followed by plasmoquine. In view of the shorter course of treatment involving a briefer stay in hospital the latter combination is more generally favoured in the military hospitals. This method of treatment is supplemented in some instances by quinine alone for the first 48 hours, with a view to the more rapid reduction

in temperature, which in certain cases occurs with quinine. On the other hand certain medical specialists with great experience in both methods of treatment, have expressed the view that as long as pyrexia causes no anxiety, preliminary quinine is unnecessary, and that patients, to whom quinine is not administered initially, look fitter at the end of their course of treatment.

#### Enteric group of fevers

The incidence for British troops is well below that of 1934, which was the lowest ever recorded, and less than half that of 1936 which was also low. The reduction in the number of paratyphoid A cases is also welcome as in the past few years the total cases, although comparatively few, had not diminished in similar proportion to the typhoid cases.

Three deaths occurred among the typhoid cases (two broncho-pneumonia, one severe bronchitis and myocarditis).

The incidence among Indian troops was not as low as in 1936 although less than half that in 1934, the record year at that time. Enteric fevers were severe in many parts of India during the year, particularly in the Punjab, and the seven typhoid and nine paratyphoid cases more than in 1936 undoubtedly reflect the incidence among the civil population with whom naturally contact is greater among Indian than British troops. Several of the infections were actually contracted while on leave in villages.

#### Fevers of the typhus group

Twenty-nine cases occurred among British troops as compared with 44 in 1936. In addition 43 cases were diagnosed among Indian other ranks, four less than in 1936. Again the cases fall into the two main groups of scrub typhus (*Proteus* OXX) and urine typhus (*Proteus* OX 19), with a smaller number giving definite diagnostic high titres of agglutination to *Proteus* (OX 2); finally an even smaller number in which although the clinical symptoms were typical no adequate serological evidence was obtained, or else a general rise in agglutination titre prevented definite classification.

#### Dysentery, diarrhoea, colitis and amœbic hepatitis

The dysentery admission ratio for all-India has again slightly increased by 0.9 per 1,000. Concurrently the diarrhoea and colitis group were slightly reduced, bringing the ratio of admissions for this whole group similar to that of previous years. Commands showing increased dysentery figures were Northern, Eastern and Southern. In Western Command although there is a reduction on the previous year's figures, the ratio per 1,000 was still high (28.44 per 1,000).


#### Effects of heat

In 1937 there were 15 cases (0.3 per 1,000) of heat stroke with six deaths and 37 cases (0.8 per 1,000) of heat exhaustion with two deaths. In 1936 there were 13 cases (0.2 per 1,000) of heat stroke with three deaths and 39 cases (0.7 per 1,000) of heat exhaustion with one death.

Heat stroke and heat exhaustion cases responsible for many catastrophes among British troops some years ago have been considerably reduced in number. This group numbered 212 in 1926. In 1937 there were 52. There is less tendency now to shut up troops during the hot hours of the day, and the modern soldier has little interest in alcoholic liquors, as compared with his forebears. Both factors are probably concerned in reducing the incidence of these cases.

#### Dengue and sandfly fever

*Dengue.*—There was a very marked increase in the total amount of dengue fever during the year but this was due to an epidemic in Calcutta which started in July and continued up to the end of October. Calcutta being in the Ganges delta and near the coast is subject to periodic epidemics of dengue and the last occurred in 1931.



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There were a few sporadic cases in April, May and June but in the middle of July the numbers increased. The epidemic reached its peak in September and subsided by the end of October.

About 40 per cent of the British troops in Calcutta were affected and 237 of the British cases occurred in Port William. Indian troops in Alipore were affected but to a much less extent. Many civilians living in Calcutta were also victims of the epidemic.

**Sandfly fever.**—The very marked reduction in the incidence of this disease was due largely to the decrease in Northern Command where intensive anti-sandfly measures were carried out during the year. The Assistant Director of Hygiene and Pathology, Northern Command, reports that the greatest reduction occurred at stations where the campaign was most intensive, the exceptionally good results at Landikotal having followed a most conscientious application of active sandfly measures.

#### *Oriental sore*

There were only 12 cases among British troops in 1937 but there were 132 cases among Indian troops. This is a considerable reduction on last year when there was an epidemic in Quetta. This year there were only one British and three Indian cases in Quetta.

#### *Cysticercosis*

Four cases occurred among British troops during the year of which two were at Secunderabad and one each at Jhansi and Peshawar. Two of these cases were invalided, and two have been kept under observation. One of the cases had a previous history of *Tania saginata* infestation in 1930, presumably an incorrect diagnosis. The three other cases gave no history of previous tape worm infection.

#### *Diphtheria*

There were no epidemics of any size. In Peshawar 12 cases occurred in the autumn, and 12 were also reported from Waziristan. The greater number of cases were from Southern Command and small outbreaks continued in Poona and Kirkee among the school children. Active immunization of the children with T. A. F. was continued from 1936. One case of diphtheria unfortunately occurred in an immunized child which somewhat discredited the process in the eyes of parents. There was one death in a child in Belgaum, which was seen for the first time when

stridor had developed after a two-day history of sore throat. The child died after tracheotomy had been performed, but a laryngeal swab *post mortem* was positive to virulent *C. diphtheriae*. Only two cases occurred among Indian other ranks during the year, a striking difference to the annual numbers of cases among British troops and families.

#### *Cerebro-spinal fever*

Only one case occurred among British troops (Ranikhet) during the year. The case recovered. Another case was reported from Cawnpore, but although an undoubted meningitis, it was not caused by the meningococcus.

There were 17 cases among Indian other ranks and five among followers, the total being the same as in 1936. Thirteen of these cases died. Twenty-one of the cases were treated with Lister Institute concentrated serum.

#### *Smallpox*

There were thirteen cases of smallpox in 1937 compared with eight in 1936. There were seven cases and one death among British other ranks, two cases and no deaths among British officers' wives, two cases and one death among British other ranks wives and two cases and no deaths among British other ranks children. All had been vaccinated, but in two cases repeated vaccination had been unsuccessful. Of the two cases that died the British other rank had been vaccinated in 1936, but the British other rank's wife had been vaccinated only at birth.

#### *Respiratory diseases*

The admissions for respiratory diseases were slightly higher than in the previous year, being 24.2 per 1,000 in 1937 compared with 23.2 per 1,000 in 1936. There were 101 cases of lobar pneumonia with only two deaths as against 132 cases and 14 deaths in 1936. The incidence of lobular pneumonia and pleurisy showed little change, but there were fewer cases of bronchitis.

#### *Tuberculosis*

There were 61 admissions for pulmonary tuberculosis and seven for tuberculosis other than pulmonary, compared with 57 and nine respectively in the previous year. One death occurred from pulmonary tuberculosis. The cases were evenly distributed throughout India and there was no particular unit with undue prevalence.

## Correspondence

### CHRONIC SNAKE-BITE

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—The letter in your June number about the chronic snake bites was read by me with great interest. I have heard of a large number of such cases myself. One of my own relations was bitten year after year by snakes for many years. I have recorded many cases similar to the one mentioned in the *Indian Medical Gazette*.

Such incidents are heard very commonly in the Punjab. I have been trying to enquire if any such incidents are reported in Bengal and Madras, where also poisonous snakes abound; but so far nobody has reported any cases similar to chronic snake bites in these provinces. Is it possible that certain type of snakes which gives such bite are only isolated in the Punjab? In the Punjab, it is alleged that a particular type of snake known as *Do-muhan* (meaning double headed in which both the caudal and cephalic ends look like heads) is responsible for such bites. This snake is said to be a non-poisonous female snake. If this type of snake bites particularly during her heat (mating season) or during egg-laying period then the

victim is bitten repeatedly during that period every year, and in worse cases even on the same dates every month. Some persons allege the bite is influenced by particular phases of the moon. It is said that during that period a particular type of smell is emanated by the victim which attracts male snakes exactly as if they would be attracted by a female snake during her mating season. The male snake therefore comes and inflicts a non-fatal bite to the person. The usual treatment suggested to their victims is said to be *mantras* (charms) by the snake charmers or tying a snake stone as an amulet, etc. An amulet may be made of the skin of *Mar-khor* (a type of snow deer which eats snakes) or taming of mongoose. Snakes have a great fear and aversion for all these and so leave the victim for good.

Whether all these are only fibs or there is any spot of truth in it is difficult to say. I would appreciate it very much if readers would enlighten and inform me if they have heard such stories. Information on the following points will be appreciated. (1) What is a *Domuhan snake*? (2) Is it male or a female and of what species? (3) I will be very glad to have such a specimen for identification and classification, if anybody

could send me one. (4) Is the subsequent bites to those victims from a special species of snake? (5) What is their sex, and are they poisonous or non-poisonous? (6) Is it possible for the victim to acquire any *ophitactic* properties and attract snakes periodically?

Recently I had a patient, a German lady, 35 years age, who was bitten by an *Echis carinata* snake on the dorsum of foot, through woollen socks at midday in Bombay. A tourniquet was applied and the wound was sucked, but by the time she reached in hospital her feet and leg were swollen and later on her left side of the body and left side of face was swollen, followed by mild paralysis of the latter. Since then she has been feeling much pain in the legs and her limbs are weak and shaky. Another curious phenomenon noticed by her is that since lately she has been not only dreaming of but actually seeing lots of snakes. In her own words, she attracts snakes. She has seen snakes in her own house, on the golf links, etc., and in places where snakes were never noticed before. She came to the Calcutta School of Tropical Medicine for treatment. She was given six injections of cobra venom from 1 to 10 mouse units followed by another course of six after a fortnight's rest. Her pain disappeared and she has seen no snake since the treatment, for over six months.

It is possible that if any such *ophitactic* tendency has been developed in her it has been cured by small doses of venom which act as substitute to actual snake bites or by developing antiserum in her. Her pain was also relieved due to neurotoxic action of snake venom.

Yours, etc.,

J. S. CHOWHAN,

CAPTAIN, M.B., B.S., A.I.R.O.

BIOCHEMICAL STANDARDIZATION  
LABORATORY,  
ALL-INDIAN INSTITUTE OF  
HYGIENE,  
CALCUTTA,

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I have to refer you to page 380 of your *Gazette* of June 1939 where a case of Mr. P. L. is reported. I have a similar female case in my family. She has had 16 bites and continues to have them at intervals of sometimes a year, sometimes six months, and recently only a month.

Will you please inform me if you have received any useful suggestions.

Yours, etc.,

BISHAN DASS.

PATHANKOT,  
PUNJAB,  
15th November, 1939.

(Extract from *Chapel Hill Weekly*, Chapel Hill,  
North Carolina, dated 29th September, 1939)

**MRS. BROWN, SORRY FOR MAN IN THE PUNJAB,  
SAYS SNAKES WON'T BITE HIM ANY MORE IF  
HE'LL RUB HIMSELF WITH OIL OF PENNYROYAL.**

THIS newspaper published last week a letter from the *Indian Medical Gazette* of Calcutta, India, sent us by Dr. William P. Jacocks, which told of a man in the province of the Punjab, a relative of one Ishar Das, who was bitten by a snake every month in spite of various precautions. 'I most earnestly request,' Mr. Das wrote, 'that you will kindly help me in recommending any treatment for this complaint'.

The editor of the *Gazette* appended to Mr. Das's letter the note: 'We invite opinions, including those of psychologists.'

We haven't received any opinions from psychologists yet, but Mrs. Inez Brown, who lives on Columbia street at Mrs. Wallace Patterson's, called up yesterday and said that she knew why Ishar Das's relative was being regularly snake-bitten and that she'd be glad to explain it to a representative of the *Weekly*.

'Fear is the answer', Mrs. Brown said, when I was seated near her in a comfortable rocking chair on

Mrs. Patterson's porch. The letter spoke of the man's 'fear of being bitten'. Any expert animal trainer will tell you that when a man is afraid he gives off an odour of fear which is easily detected and recognized by animals and reptiles.

'Fear is the most contagious of the emotions, and when an animal detects fear in a man it becomes excited and is likely to attack. That is why normally friendly dogs often attack people who fear them, and it is believed to be the explanation of why the Hopi Indians can handle, without being bitten, deadly rattlesnakes which would kill a white man. The Indians are not afraid and therefore the snakes are not afraid and can be handled.

'Lawrence Trimble, who has made a fortune training dogs for the movies, was dreadfully afraid of them until he read or heard about the contagious odour of fear. He then began schooling himself not to fear dogs, and it was after he had lost fear that he became a famous dog trainer.

'It was no doubt a coincidence that Mr. Das's relative was first bitten at regular intervals. But it made him expect to be bitten every month thereafter, and his consequent fear of being bitten caused him to give off the scent of fear, and that scent is what is causing the snakes to bite him.

'A friend of mine in New York state was similarly troubled by snakes biting her. She was never able to overcome her fear, but she read that the scent of oil of pennyroyal would destroy the scent of fear, and she tried it and was not bitten any more.

'When I read the letter in the *Weekly* I called you up because I felt so sorry for the poor fellow in India, and I wanted to let him know what would help him. The snake will quit biting him if he will rub himself with oil of pennyroyal whenever he begins to fear he is about to be bitten. And, in time, he may lose his recurrent fear and its accompanying fear odour and may then stop using the pennyroyal.

'If you put this in the *Weekly* I hope Dr. Jacocks sees that it gets to Ishar Das and that Ishar Das shows it to his unfortunate relative.'—JOE JONES.

## A CURE FOR SCORPION STINGS

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I have read with great interest the letter of Dr. Mudaliar that has appeared under the above heading in the November 1939 issue (p. 715) of your journal.

About 18 years ago when I was at Banbassa (Terai forest) in connection with the Sarda Canal works, I came across many hundreds of cases of scorpion sting. Almost every day dozens of men from the labouring class used to come smitten with intense pain caused through the sting of this venomous creature. Scorpions abounded in that region and some of them were indeed very big (9 to 10 inches in length) and dark in colour. The people there used to fear these insects as much as they did the snakes. The symptoms varied widely in severity from mere local pain and burning to the most excruciating pain of a radiating character with severe constitutional disturbance. It was pitiful to see some of them writhing with pain and actually rolling on the ground in agony.

I gave extensive trial to most of the remedies commonly recommended for the purpose, *viz.*, solution of ammonia, phenyl, permanganate of potash, paste of ipecacuanha root, and injection of cocaine. The last remedy was found to be the only one which could be called satisfactory, provided the injection was given quite close to the site of the sting. For experience I found that this was not always possible, as in a severe case the pain was so intense and diffuse that it was not usually possible to locate the exact site of the sting.

It was by chance that I found out a very simple remedy for this painful condition. While treating a severe case of scorpion sting, all the methods that I knew at that time, including the injection of cocaine, proved futile. Then I decided to put him under

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chloroform, as he was beginning to show signs of severe constitutional disturbance, viz., convulsion, hurried breathing, exhaustion, etc. To my great surprise I found that after a few whiffs of chloroform all the symptoms—distress and pain—vanished like magic, and there was no need to push the chloroform any further to induce general anaesthesia. The relief was so prompt and complete that I could hardly believe my eyes. To convince myself I tried this method again in the next few cases with the same amazing result.

From that time onward I have used this simple remedy in many hundreds of cases with uniform success. I would invite your readers to give this method a fair trial.

The most interesting point about the treatment is that a very small quantity of chloroform is required to effect a cure. About 2 drachms will be sufficient to give relief to more than fifty patients. I usually keep a little chloroform in a small phial and ask the patient to inhale it a few times from the phial until he gets complete relief. This does not take more than 30 seconds.

I have tried ether and alcohol in the same way but have not found them so effective.

Yours, etc.,

G. GHOSH, M.B., B.S., D.T.M.

S, MINIO ROAD,  
ALLAHABAD,  
26th November, 1939.

#### M. & B. 693 IN INDIAN STRAINS OF MALARIA

To the Editor, THE INDIAN MEDICAL GAZETTE  
Sir,—I will be very glad if you will kindly allow me some space in your esteemed journal to say something about M. & B. 693 in the cases of malaria. I have gone through the article 'M. & B. 693 in Indian Strains of Malaria' in the *Indian Medical Gazette*, Vol. LXXIV, November 1939. The authors have said that M. & B. 693 has definite action on malarial parasite if continued for 5 to 6 days in doses 4 gm. daily. But may I ask you why malarial parasites

become positive after treating pneumonia by M. & B. 693, although the course of treatment continued for 5 days and in all 30 tablets were given in each case? I like to mention here three cases who were attacked with pneumonia, aged 25 years to 30 years, and who complained of fever, pain in the chest and cough. On examination I found temperature 103°F., pulse 120 per minute, respiration 55 per minute. The lower lobe of the right lung showed signs of consolidation and scattered râles and rhonchi all over the lungs. I have treated them with M. & B. 693. The treatment began in the following way, at the beginning 4 tablets at a time every 4 hours for 12 hours, then 2 tablets at a time every 4 hours for 12 hours, then one tablet thrice daily for 4 days. In all cases the temperature dropped down to 97°F. within 24 hours and ran normal as long as the course of M. & B. 693 was continued. But the day when the treatment is stopped they all had sudden rise of temperature up to 104°F. Blood was taken for malarial parasites and in each case malignant tertian parasites were positive. Then they were treated with atebrian and were cured.

In all cases total days treatment with M. & B. 693 was 5 days and in each case 30 tablets of M. & B. 693 were given by oral administration.

I am very much grateful to Dr. E. G. Michaelson, M.B. (Aberdeen), Group Medical Officer, Chulsa Medical Association, for his kind help and advice in all these cases.

Yours, etc.,

KANAI LAL CHATTERJEE, L.M.F.

MOORTEE TEA ESTATE,  
MATELLI P. O. (DOOARS),  
28th November, 1939.

[Note.—There does not seem to be any contradiction here. In the paper in our November issue it is stated that daily doses of 4 grammes each for 5 or 6 days (= 20 to 24 grammes or 40 to 48 tablets) caused disappearance of malarial parasites: our correspondent only gave 30 tablets.—Editor, I. M. G.]

## Service Notes

### APPOINTMENTS AND TRANSFERS

THE VICEROY AND GOVERNOR-GENERAL has been pleased to make the following appointments on His Excellency's personal staff, with effect from the dates stated:—

#### To be Honorary Surgeons

Colonel H. Stott, O.B.E., vice Major-General G. G. Jolly, C.I.E., K.H.P., vacated. Dated 30th August, 1939.

Colonel E. S. Phipson, C.I.E., D.S.O., vice Colonel J. Taylor, C.I.E., D.S.O., vacated. Dated 30th August, 1939.

Colonel F. F. S. Smith, vice Colonel J. A. S. Phillips, C.I.E., K.H.P., vacated. Dated 6th October, 1939.

Colonel E. G. Kennedy to be A. D. M. S., Madras District. Dated 22nd October, 1939.

Colonel J. S. S. Martin to be Officiating A. D. M. S., Deccan District. Dated 22nd September, 1939.

Colonel A. C. Macrae to be O. C., Indian Military Hospital, Rawalpindi. Dated 1st October, 1939.

Colonel G. R. Lynn, D.S.O. (Retired), to be O. C., I. M. H., Jubbulpore. Dated 30th September, 1939.

Brevet-Colonel J. W. Vanreenan, O.B.E., to be O. C., C. I. M. H., Abbottabad. Dated 3rd October, 1939.

Lieutenant-Colonel N. D. Puri, Inspector-General of Prisons, Punjab, has been advanced to the higher position of his rank (selected list), with effect from the 17th August, 1939.

Lieutenant-Colonel R. K. Tandon to be O. C., I. M. H., Allahabad. Dated 8th September, 1939.

Lieutenant-Colonel D. V. O'Malley, O.B.E., to be O. C., I. M. H., Sialkot. Dated 1st October, 1939.

Lieutenant-Colonel R. V. Martin, C.I.E., to be O. C., C. I. M. H., Wana. Dated 23rd October, 1939.

Lieutenant-Colonel R. Lee to be O. C., I. M. H., Meerut. Dated 1st October, 1939.

Lieutenant-Colonel P. Savage to be O. C., I. M. H., Bareilly. Dated 30th October, 1939.

Lieutenant-Colonel H. Das to be O. C., I. M. H., Delhi. Dated 30th September, 1939.

Lieutenant-Colonel I. S. Nalwa, Officiating Inspector-General of Prisons, on transfer, made over, and Lieutenant-Colonel J. Findlay on being recalled to duty received charge of the duties of the Inspector-General of Prisons, Burma, on the afternoon of the 3rd October, 1939.

Lieutenant-Colonel G. C. Maitra made over and Lieutenant-Colonel R. H. Malone, on being recalled to duty, received charge of the duties of Pathologist, General Hospital, Rangoon, and Lecturer in Pathology, Burma Government Medical School, on the forenoon of 3rd October, 1939.

Lieutenant-Colonel W. J. S. Ingram, on being recalled to duty, assumed charge of the 'Civil Surgeoncy' at Prome on the afternoon of the 5th October, 1939.

Lieutenant-Colonel J. H. Barrett, on being recalled to duty, assumed charge of the duties of the Civil Surgeon, Mergui, on the forenoon of the 13th October, 1939.

Lieutenant-Colonel J. P. Huban, O.B.E., an Agency Surgeon, is employed as the Administrative Medical Officer in Rajputana, with effect from the forenoon of the 30th October, 1939.



Lieutenant-Colonel R. F. D. MacGregor, C.I.E., M.C., is appointed to officiate as Chief Medical Officer and Civil Surgeon, Delhi, with effect from the 2nd November, 1939 (forenoon), until further orders, *vice* Major J. A. W. Ebdon, I.M.S. (since deceased).

Major D. Kelly, Civil Surgeon, Raipur, is transferred as Civil Surgeon and Superintendent, Robertson Medical School, Nagpur.

Major V. E. M. Lee to be O. C., I. M. H., Bakloh. Dated 2nd October, 1939.

Major T. A. Malone to be D. A. D. M. S., A. II. Qrs. Dated 3rd September, 1939.

Major G. Dockery was transferred to the Semi-Effective List. Dated 18th September, 1939.

Major T. C. Puri to be D. A. D. P., Peshawar District. Dated 21st September, 1939.

Major H. W. Farrell, an Officiating Agency Surgeon, is employed as C. M. O., and Inspector-General of Prisons in Baluchistan, with effect from the forenoon of the 4th October, 1939.

Major E. A. O'Connor, an Officiating Agency Surgeon, is appointed as Civil Surgeon, Quetta-Sibi, with effect from the forenoon of the 5th October, 1939.

Major G. J. Smith made over and Captain H. B. MacEvoy received charge of the executive and medical charge of the Insein Central Jail, on the forenoon of the 5th October, 1939.

Major P. A. C. Davenport, on transfer, received charge of the executive and medical charge of the Mandalay Central Jail, on the forenoon of the 10th October, 1939.

Major R. McRobert, on being recalled to duty, assumed charge of the duties of the Civil Surgeon, Monywa, on the forenoon of the 12th October, 1939.

On return from China, Major K. Rai joined the I. M. H., Lansdowne, for duty, on 30th October, 1939.

On the completion of his tour of duty at Murree, Major B. Temple-Raston assumed charge of the office of Civil Surgeon, Attock District, Campbellpur, on the afternoon of the 3rd November, 1939.

Captain F. C. Leach, Civil Surgeon, Saugor, is transferred as Civil Surgeon, Raipur.

Captain J. W. R. Sarkies joined military employ in Burma, on the 14th September, 1939.

The undermentioned short service R. A. M. C. Officers have been granted permanent commissions in the I. M. S.:—

Captain F. J. O'Dowd. Dated 25th September, 1939.

Captain C. S. Gamble. Dated 20th October, 1939.

Captain J. G. Stonham reverted from Civil Burma. Dated 29th September, 1939.

Captain J. H. Cater to be Officer-in-Charge, Brigade Laboratory, Bannu. Dated 29th September, 1939.

Captain W. W. Laughland to be Mental Specialist, Eastern Command. Dated 1st September, 1939.

Captain J. G. Stonham to be Specialist in Ear, Nose and Throat Diseases, Southern Command. Dated 1st October, 1939.

Captain E. J. Somerset to be Specialist in Ophthalmology, Western (Ind.) District. Dated 26th October, 1939.

Captain H. B. MacEvoy made over and Lieutenant-Colonel I. S. Nalwa received executive and medical charge of the duties of the Rangoon Central Jail, on the forenoon of the 4th October, 1939.

*New Appointments:*—Captain R. L. Raymond, Ophthalmic Surgeon, General Hospital, Rangoon, on transfer, made over and Lieutenant-Colonel H. S. Cormack, I.M.S., on being recalled to duty, received charge of the duties of Ophthalmic Surgeon, General Hospital, Rangoon, on the forenoon of 3rd October, 1939.

Captain J. Morgan reverted from military Burma. Dated 5th October, 1939.

Captain H. W. G. Staunton, an Officiating Agency Surgeon, is appointed as Additional Medical Officer, Central India, with effect from the afternoon of the 8th October, 1939.

Captain R. L. Raymond, on transfer, assumed charge of the duties of the Civil Surgeon, Magwe, on the forenoon of the 12th October, 1939.

Captain R. D. MacRae, an Officiating Agency Surgeon, on return from leave, is appointed as Agency Surgeon, Gilgit, with effect from the afternoon of the 12th October, 1939. The unexpired portion of his leave is hereby cancelled.

Captain M. S. Purvis, on being recalled to duty, assumed charge of the duties of Civil Surgeon, Shwebo, on the 13th October, 1939.

On completion of his tour of duty at Dalhousie, Captain C. F. Garfit, assumed charge of the Office of Civil Surgeon, Jhelum, on the forenoon of the 1st November, 1939.

On transfer from Sargodha, Captain D. W. Taylor was placed on special duty at the Mayo Hospital, Lahore, with effect from the 9th November, 1939.

Lieutenant (on probation) A. S. Brown is restored to the establishment on 1st September, 1939, with seniority from 1st September, 1938.

The undermentioned newly appointed I. M. S. Officers have arrived in India for duty:—

Lieutenant K. D. Fraser.

Lieutenant J. Aitken.

Lieutenant H. Rees.

Lieutenant D. S. Wilson.

Lieutenant R. O. Yerbury.

Lieutenant D. H. Harrison.

Lieutenant G. T. M. Hayes.

Lieutenant P. Kent.

Lieutenant G. S. Michelson.

Lieutenant W. M. McCutcheon.

Lieutenant P. J. Wormald.

Lieutenant J. P. O'Riorden.

Lieutenant S. G. Nardell.

Lieutenant A. S. Brown.

Lieutenant W. P. D. Griggs.

The Secretary of State for India has appointed to the Civil Branch of the Indian Medical Service the following Officers of the Indian Medical Service, with effect from the dates stated against their names:—

#### *Central Government*

Captain C. J. Hassett. Dated 3rd January, 1939.

Major G. Milne. Dated 18th January, 1939.

Major J. H. Gorman. Dated 6th February, 1939.

Captain H. W. G. Staunton. Dated 28th March, 1939 (afternoon).

Captain T. Somerville. Dated 30th May, 1939 (afternoon).

#### *Madras*

Captain S. Shone. Dated 17th January, 1939 (afternoon).

#### *United Provinces*

Captain A. B. Guild. Dated 14th January, 1939.

Captain T. F. O'Donnell. Dated 6th April, 1939.

#### *Punjab*

Captain D. W. Taylor. Dated 1st June, 1939.

#### *Bihar and Orissa (joint cadre)*

Captain A. T. Andreasen. Dated 13th April, 1939 (afternoon).

Captain J. D. Murdoch. Dated 9th May, 1939.

The Secretary of State for India has sanctioned the reversion to military employment of the following officers of the I. M. S. (Civil), with effect from the dates mentioned against their names:—

#### *Central Government*

Lieutenant-Colonel R. L. Vance. Dated 12th November, 1937.

Lieutenant-Colonel W. M. Will. Dated 31st October, 1938 (afternoon).

Captain C. J. H. Brink. Dated 27th November, 1938.

Colonel E. G. Kennedy. Dated 20th April, 1939.

#### *Madras*

Major J. S. McMillan. Dated 1st September, 1937.

Lieutenant-Colonel C. S. V. Ramanan. Dated 6th November, 1937 (afternoon).

#### *Bombay*

Captain P. I. Franks. Dated 29th October, 1937 (afternoon).

Captain W. W. Laughland. Dated 4th June, 1938.

# **Physiological action of BOVRIL**

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Following most acute illnesses there is commonly a depression of gastric secretion, and the secretion is poor in hydrochloric acid. In such cases Bovril helps by stimulating the gastric mucosa and restoring the gastric juice to normal, both in volume and activity.

\**B.M.J.*, 1937, August 28. Page 412.

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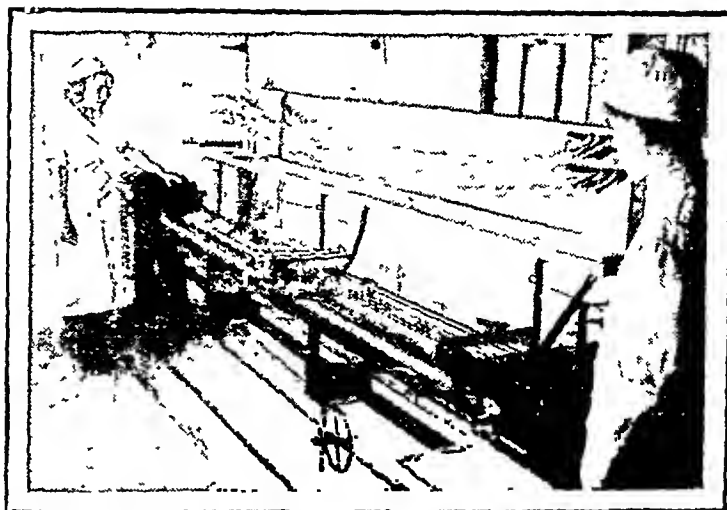
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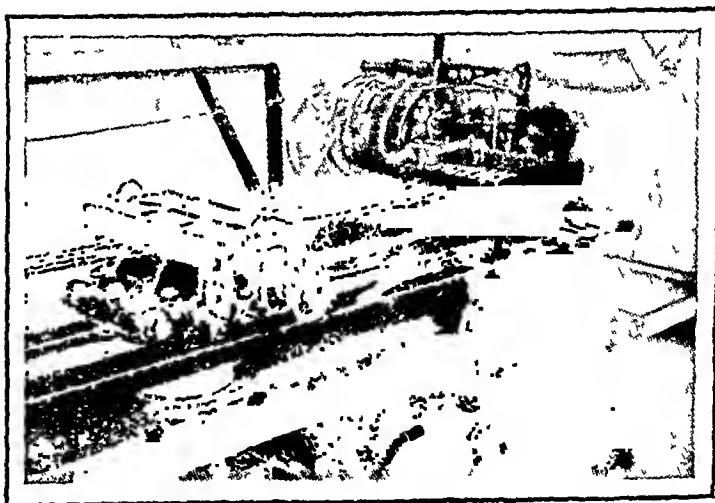
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*Bengal*

Lieutenant-Colonel R. E. Flowerdew, c.i.e. Dated 25th May, 1937.

Major B. N. Hajra. Dated 14th February, 1938.

Major A. K. Gupta. Dated 14th February, 1938.

*United Provinces*

Lieutenant-Colonel B. R. Chaudhri. Dated 17th April, 1939.

Captain Jaswant Singh. Dated 10th September, 1937.

Major R. D. Alexander. Dated 3rd August, 1938.

*Bihar*

Major G. P. F. Bowers. Dated 4th October, 1937 (afternoon).

Lieutenant-Colonel H. M. Strickland. Dated 10th November, 1937.

*Central Provinces and Berar*

Lieutenant-Colonel R. A. Logan. Dated 20th November, 1937 (afternoon).

Lieutenant-Colonel J. Carrey. Dated 4th March, 1938.

Lieutenant-Colonel J. E. Ainsley. Dated 2nd August, 1938 (afternoon).

Major V. E. M. Lee. Dated 19th August, 1938 (afternoon).

The undermentioned A. I. R. O. (Medical) Officers have been called up for service:—

Captain D. C. Aggarwal.

Captain H. S. Ahluwalia.

Captain L. S. Ahluwalia.

Captain Atyaktanand.

Captain P. R. Bali.

Captain N. D. Banerji.

Captain P. K. Banerji.

Captain D. S. Bhalla.

Captain Bhawani Dass.

Captain G. S. Bindra.

Captain B. S. Bindra.

Captain Binod Lal Tewari.

Captain Boota Singh.

Captain R. N. Bose.

Captain C. P. Chaube.

Captain K. S. Chopra.

Captain M. R. Chowdhury.

Captain D. C. Datta.

Captain K. M. Desai.

Captain L. S. Ferozepuri.

Captain D. T. P. Gay.

Captain J. S. Gill.

Captain S. K. Ghosh.

Captain S. H. Gokhale.

Captain A. S. Gupta.

Captain Harish Chandra.

Captain Ijaz Ahmad Siddiqui.

Captain Jagdev Singh.

Captain S. P. Jain.

Captain Kapila Sukhdev.

Captain M. N. Kalbagh.

Captain K. C. Kandhari.

Captain N. C. Kapur.

Captain L. R. Kapur.

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Captain A. L. Khorana.

Captain N. D. Kotwal.

Captain Khanijo.

Captain Y. N. Lal.

Captain N. G. Latey.

Captain Manohar Lall.

Captain G. D. Luthra.

Captain A. K. Maitra.

Captain Man Singh.

Captain D. P. Mehra.

Captain Mohan Singh.

Captain A. N. Narang.

Captain S. N. Narang.

Captain G. G. Naolekar.

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Captain T. R. Pahwa.

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Captain Pran Nath.

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Captain S. R. Sethi.

Captain Mohammed Sharif.

Captain G. L. Sharma.

Captain L. R. Sharma.

Captain G. S. Sodhi.

Captain A. C. Sud.

Captain R. N. Sud.

Captain Tara Singh.

Captain V. S. Trivedi.

Captain H. B. Vaid.

Captain M. C. Varma.

Captain Wazir Singh.

The undermentioned retired Officers have been recalled:—

Colonel G. R. Lynn, D.S.O.

Lieutenant-Colonel H. Hingston.

Lieutenant-Colonel R. deS. B. Herrick, D.S.O.

Lieutenant-Colonel F. Oppenheimer.

Lieutenant-Colonel C. M. Plumtre.

Lieutenant-Colonel J. A. Sinton, V.C., O.B.E.

Lieutenant-Colonel M. L. C. Irvine.

Lieutenant-Colonel F. W. Hay.

Lieutenant-Colonel J. B. deW. Molony, O.B.E.

Lieutenant-Colonel A. Kennedy.

Lieutenant-Colonel R. E. Flowerdew, C.I.E.

Lieutenant-Colonel W. O. Walker.

Lieutenant-Colonel W. J. Simpson.

Lieutenant-Colonel G. F. Graham.

Lieutenant-Colonel H. K. Rowntree.

Lieutenant-Colonel H. G. Alexander.

Lieutenant-Colonel D. McN. Taylor.

Lieutenant-Colonel S. M. Hepworth.

Lieutenant-Colonel F. Griffith.

Lieutenant-Colonel J. R. D. Webb.

Lieutenant-Colonel T. L. Bomford.

Lieutenant-Colonel H. R. B. Gibson.

Major S. Gordon, M.C.

Major M. Purvis.

Major E. Calvert.

Major R. W. G. Hingston, M.C.

Major W. J. Forsyth.

Major G. Y. Thomson.

Major V. A. Edge.

*Leave*

Major J. H. Boulbee has been granted a further extension of sick leave up to 31st January, 1940.

Major R. N. Bhandari, on 2½ months' leave from 28th October, 1939.

Major F. R. W. K. Allen, Civil Surgeon and Superintendent, Robertson Medical School, Nagpur, has been granted 6 months' leave ex-India on Medical Certificate from 6th November, 1939.

*PROMOTIONS*

The undermentioned Indian Medical Service Officer is advanced to the List of Special Selected Lieutenant-Colonels:—

Lieutenant-Colonel R. F. D. MacGregor, C.I.E., M.C. Dated 30th August, 1939.

*Majors to be Lieutenant-Colonels*

R. T. Advani. Dated 14th November, 1939.

W. C. McKee. Dated 18th November, 1939.

*Captains to be Majors*

R. C. Dracup. Dated 6th November, 1939.

B. L. Taneja. Dated 19th November, 1939.

*To be Captain (on probation)*

Francis John O'Dowd. Dated 24th September, 1939, with seniority as Lieutenant from 24th September, 1934 and as Captain from 24th September, 1935.

*Lieutenant to be Captain*

T. Maung. Dated 29th March, 1939.

## RETIREMENTS

Colonel J. A. S. Phillips, C.I.E., K.H.S. Dated 6th October, 1939.

Colonel D. C. V. FitzGerald, M.C., K.H.P. Dated 22nd October, 1939.

Lieutenant-Colonel M. D. A. Kureishi. Dated 14th October, 1939.

Lieutenant-Colonel S. A. Phatak. Dated 23rd October, 1939.

Lieutenant-Colonel F. R. Thornton, M.C. Dated 5th August, 1939.

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## Note

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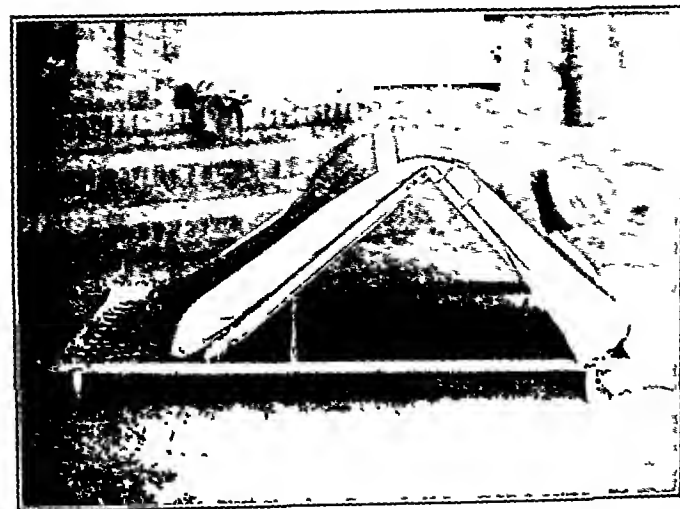
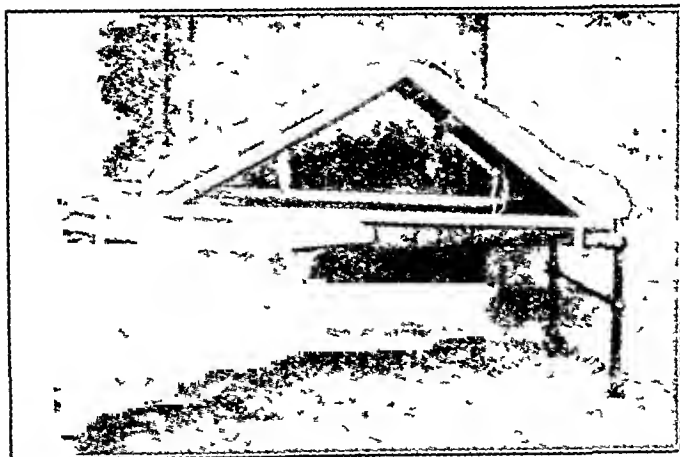


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### NOTE ON A 'NELSON BED' MADE FOR THE MAYO HOSPITAL, LAHORE BY ALLIBHOY VALLIJEE—SURGICAL INSTRUMENT MAKERS, MULTAN

THE photographs show the 'Nelson bed' frame made by Allibhoj Vallijee recently. It fits an ordinary hospital bed frame and can be made to fit any size of bed. The angle can be varied by slots in the side of the frame.

Nelson at the Brompton hospital, London, first made this type of bed for treatment of cases of bronchiectasis, and lung abscess by 'postural drainage'. The patient is strapped on the bed with his head at a lower level than his chest as shown in the photograph. He remains in this position for several hours, causing the purulent



sputum which has collected in the cavities in the lungs and bronchi to be drained from them and coughed up. Patients become accustomed to this abnormal position after a few days and are able to remain in it for many hours of the day.

In the Mayo Hospital, Lahore, it has been used for the 'wet' purulent type of bronchiectasis, and lung abscesses both conditions being fairly common here.

The cost of the bed was Rs. 60. Allibhoj Vallijee may have to increase the price because of the War.



I wish to thank Mrs Bharucha, wife of the Inspector-General, Civil Hospitals, Punjab, for collecting the money for the beds and for her enthusiasm in arranging for them to be made.

G. F. TAYLOR,

MAJOR, I.M.S.,

*Professor of Clinical Medicines.*

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## Publishers' Notice

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## Original Articles

### CIRCULATORY FAILURE IN TYPHOID FEVER

By GERARD KELLY, F.R.C.P.(I.)

MAJOR, I.M.S.

*Professor of Clinical Medicine, Medical College Hospitals, Calcutta*

IN a former paper reference was made to the central contribution to circulatory failure in typhoid fever made by myocardial weakness due to toxæmia and to impairment of the coronary circulation by severe grades of peripheral failure (Murray and Kelly, 1938). Peripheral failure in typhoid fever, and the total clinical picture of circulatory failure in severe cases will be the subjects of the present communication.

An insufficient blood flow to the body is responsible for the main clinical features of circulatory failure in typhoid fever. Hence we may briefly recall the conditions necessary for an adequate blood supply to the tissues. The primary requisites for an adequate blood supply to the tissues are a normal cardiac income and normal contractile power of the cardiac pump. The filling of the heart is dependent upon the venous pressure which usually rises and falls with increase and decrease, respectively, of the circulatory blood volume. The blood supply to the heart and brain depends mainly upon the arterial blood pressure. And the arterial blood pressure in turn is a function chiefly of the output of the heart and of the peripheral resistance. The tone of the arterioles determines the peripheral resistance. Fishberg (1937) states that the blood pressure is more readily influenced by changes in the calibre of arterioles than by variations in the output of the heart or in the viscosity of the blood. The cardiac output is controlled by three factors, namely (1) the venous return, (2) the force of the heart, and (3) the heart rate.

#### *Dual failure*

Clinically, circulatory collapse in severe typhoid fever is a dual failure, characterized by outspoken peripheral and occult central failure. On ward rounds I have repeatedly emphasized the shock-like picture presented by such cases, due to a disparity between the circulating blood volume and the functioning capacity of the vascular bed. 'In peripheral failure the circulating blood volume is diminished and the capacity of the vascular bed is increased with resultant pooling of blood in the periphery' (Fishberg, 1937). With this decrement in the circulating blood volume, there is a corresponding fall in the venous pressure with consequent decrease in the cardiac output, which is further reduced, because

of the impairment of contractility of the heart due to typhoid myocarditis. To combat the resultant steep fall of blood pressure the decrease in circulating blood volume provokes constriction of the peripheral arterioles. The cold clammy skin is due, according to Harrison (1939), to diminished blood flow to the skin because of the decline in the cardiac output and the local vaso-constriction. The grey cyanosis (pallor *plus* cyanosis) proclaims stagnation of blood at the periphery. In the dual failures of typhoid fever and coronary thrombosis (Levine, 1929), the coldness of the skin affords a striking contrast to the high rectal temperature obtainable in these cases. Circulatory collapse in enteric is not to be attributed to vaso-motor paralysis, which is the result, rather than the cause, of the fall of blood pressure. When the latter falls below 60 or 70 mm. the vaso-constrictor mechanism fails owing to ischæmia of the vaso-motor centre, vaso-dilatation supervenes and a further final fall in blood pressure results. Death ensues in a few hours if the blood pressure is not successfully restored to an adequate level. Impending circulatory failure is usually notified at an earlier stage in the temperature chart, which shows replacement of the characteristically slow pulse by a tendency to tachycardia linked with decline in the height of the fever. About the same time there may be a slight rise in blood pressure due to peripheral vaso-constriction, which rise in the blood pressure is to be interpreted as the prelude to a sharp fall.

Feeble pulse, rapid heart rate, distant heart sounds and even foetal heart sounds occur equally in peripheral failure and in acute myocarditis. The changes undergone by the first heart sound in severe enteric fever, however, are to some extent due to a coexisting myocarditis. Temporary gallop rhythm is even more suggestive of a transient myocardial weakness. In grave circulatory collapse the heart sounds may be almost inaudible, the blood pressure unregistrable, the pulse almost or quite impalpable and the superficial veins totally collapsed. The development of an apical systolic murmur suggests acute cardiac dilatation. The development of cardiac enlargement under radiological observation would constitute direct evidence of acute myocarditis. Unfortunately, such a radiological study of the heart in typhoid is rarely possible. Fishberg (1937) tells us that—'the heart is not enlarged in pure shock. On the contrary there is every reason to believe that characteristically the heart diminishes in size as a result of the deficient filling due to the small venous returns'. Most commonly in severe cases the typhoid heart gives the palpating finger the impression of at least a full-sized heart, even after allowing for upward diaphragmatic displacement by the commonly prevailing meteorism and after exclusion of other possible causes of cardiac enlargement such as hypertension, organic valvular disease, etc. 'Electrocardiographic evidence of myocardial damage is not



rare' (Fishberg, 1937), especially prolongation of the P-R interval and T-wave inversion in lead II and sometimes in lead I also. Such T-wave changes are to be differentiated from those due to digitalis by the fact that the QRS is followed by a horizontal or upwardly-convex RS-T segment which in turn is followed by the inverted T.

### *Prognosis*

Within the past six months we have had three cases of severe typhoid fever with circulatory failure as described above. Two of the cases, males aged 24 and 30 years, respectively, of average constitution, made a good recovery without further complications of note. The third case, an obese man of 40, terminated fatally: 48 hours before death two of his stools were tinged with blood but the third and last stool was blood-free.

The prognosis is favourable in previously healthy young people. Middle-aged and elderly subjects, and more especially those who are obese as well, frequently succumb to the circulatory failure of typhoid fever.

### *Summary of treatment*

The aim of treatment in the circulatory failure of typhoid fever is obviously to increase the volume of the circulating blood, to decrease the capacity of the vascular bed and to diminish cerebral anæmia.

#### *Increase the volume of the circulating blood*

Intravenous glucose saline, by the drip method, in view of the state of the heart, is the most certain procedure in the circulatory collapse of typhoid fever. We give subcutaneous glucose saline immediately signs of impending circulatory failure appear: in profound circulatory depression absorption by this route is inadequate.

In toxæmic peripheral failure cortin helps to prevent water and salt depletion and thus inhibits the rise in serum potassium associated with concentration of the blood. Thomson (1939) demonstrated the toxic action of potassium salts, particularly on the myocardium, and rightly advises against the use of potassium salts in cases of cardiovascular disease and chronic nephritis, the commonest conditions in which potassium citrate has been hitherto prescribed. The suprarenal cortex, moreover, contains ascorbic acid (or vitamin C) which helps to restore normal capillary resistance. In Addison's disease the chloride content of the body is characteristically low, hence sufferers from this affection receive a daily ration of sodium chloride as part of their routine treatment; intravenous 5 per cent NaCl with glucose is effectively employed in the crisis of Addison's disease. In 1936, Bernhardt stated that he found intravenous cortical hormone and vitamin C more effective than camphor, cardiazol or

coramine in the circulatory collapse of malignant diphtheria. He used intravenous injections containing the following:—

Adrenal cortical hormone	..	10 c.cm.
Vitamin C preparation	..	2 "
Glucose (10 per cent)	..	20 "
NaCl (5 per cent)	..	5-10 "

Small repeated doses are better than a single large one. This procedure should be followed immediately the enteric case manifests signs of impending circulatory failure.

Deficiency of vitamin B<sub>1</sub>, according to Weiss and Wilkins (1936), tends to produce hypersensitivity of the carotid sinus reflex and consequently attacks of peripheral vaso-dilatation with faintness or unconsciousness, which attacks do not seem to be a feature of the circulatory collapse of typhoid.

#### *Decrease the capacity of the vascular bed by vaso-constrictor drugs*

In view of the existing constriction of the peripheral arterioles, the physician must not rely overmuch upon vaso-constrictor drugs, such as adrenalin, ephedrine, camphor in oil and caffeine sodium benzoate, to mention those employed in our wards. We generally give them parenterally in rotation at say six-hourly intervals, in each case according to requirements.

*Other drugs.*—The general practitioner of to-day employs coramine in all conditions of circulatory adversity. Coramine has at least ousted the practitioner's old-time favourite in circulatory emergencies, namely, the hypodermic injection of digitalis and strychnine. As may be expected in predominantly peripheral circulatory failures, the main indication for digitalis therapy, that is congestive heart failure, is clinically invident in the vast majority of enteric cases with circulatory collapse. Digitalis actually decreases the circulating blood volume and hence is emphatically contra-indicated in shock (peripheral circulatory failure) due to any cause. Moreover, when a patient is febrile, the efficiency of digitalis is impaired even in the presence of downright indications for its employment. It may even be harmful to the myocardium already damaged by the toxæmia of enteric fever. Finally, according to Johnson and Gilbert (1931) a hazard of sudden death attends the use of ephedrine in cases receiving digitalis: these observers advise extreme caution in the use of adrenalin in such circumstances. And adrenalin is the most reliable of all drugs in cardiovascular emergencies. We never use strychnine in the circulatory collapse of typhoid fever: for one thing it stimulates intestinal movements, for another its effective dose is heroic.

*Other measures.*—The patient should be kept as flat as possible, the pulmonary state permitting. Raising the foot of the bed and thus displacing the inflamed enteric bowel upwards with

(Continued at foot of next page)

# FURTHER LIGHT ON THE MECHANISM OF SANDFLY TRANSMISSION OF KALA-AZAR\*

By R. O. A. SMITH  
K. C. HALDER .

and

I. AHMED

(Kolo-azar Enquiry under the Indian Research Fund Association at the Darbhanga Medical School, Bihar)

THE method of re-feeding *Phlebotomus argentipes* to keep them alive under laboratory conditions for the experimental transmission of kala-azar was first described by Shortt, Barraud and Craighead (1926a) and till the inception of the present series of transmission experiments

(Continued from previous page)

resultant further elevation of the diaphragm and cardiac embarrassment is obviously an unsound procedure. We do not use the electric cradle in the circulatory emergencies of typhoid fever as, in the opinion of Fishberg (1937), it would neutralize an important defensive mechanism: besides, further sweating and loss of fluid is undesirable. Nor do we use continuous warmed oxygen unless the lungs indicate the necessity for it. The grey cyanosis arising peripherally in these cases is no sort of indication for oxygen therapy.

## Summary

1. Clinically, circulatory collapse in severe typhoid fever is a dual failure, characterized by outspoken peripheral and occult central failure.
2. Prognosis depends largely upon the patient's age and condition.
3. The rational treatment of this emergency is outlined.

I am grateful to Lieut.-Colonel J. C. De, I.M.S., Principal of the Medical College and Superintendent of the Medical College Hospitals, Calcutta, for permission to publish this paper.

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\* This work is being reported more fully in papers that will appear in the next number of the *Indian Journal of Medical Research*.

was the popular method of maintaining sandflies for the purpose. The results obtained by the method advocated were sufficient to obviate the necessity for further investigation of substances other than blood on which sandflies would feed and thrive. Perhaps the name phlebotomus itself was also in some manner responsible for the impression that these insects could not live without blood, and even attempts at the artificial feeding of sandflies involved the use of blood in some form or other.

The paucity of successful transmissions in a large number of experiments led certain workers to doubt the rôle of the sandfly in the transmission of kala-azar and to investigate methods of infection other than by an insect vector. The fact that hamsters could be infected with *Leishmania donovani* administered by the oral route (Shortt, Craighead, Smith and Swaminath, 1928) and reports of the finding of parasites in the faeces of kala-azar patients (Shortt, Smith, D'Silva and Swaminath, 1929) as well as in the nasal and pharyngeal secretions (Forkner and Zia, 1935) was evidence in support of such an hypothesis.

Others were of opinion that a study of the bionomics of *P. argentipes*, of which so little is known, would most probably lead to the incrimination of this insect as the vector; for not only was the circumstantial evidence in support of the sandfly transmission of kala-azar very strong and in complete accord with our present knowledge of the epidemiology of the disease, but more especially because a few successful transmissions had already been obtained by the bites of these flies.

Till 1934 therefore when the last series of transmission experiments were concluded, *P. argentipes* used for the purpose were kept alive on successive blood meals according to the method recommended by Shortt, Barraud and Craighead. The first and usually the second feed also was given on a kala-azar patient in order to infect the flies, and the third and subsequent feeds were on experimental animals. It was assumed that not till the flies were ready for a third feed, which was about six or seven days after the first blood meal, were flagellates present in sufficient numbers at the 'anterior station' to be inoculated into a victim at the bite of the fly.

It was reported by Smith (1936) that *P. argentipes* could be maintained successfully under laboratory conditions, either before or after a blood meal, for relatively long periods if they were fed on a five per cent solution of glucose. A serious disadvantage attendant on the method employed in feeding the flies on glucose was the rapidity with which bacteria grew in the glucose solution and infected the flies. Bacterial infections either killed the flies themselves or caused the death of the flagellates contained in their midguts. The method was therefore unsuited for keeping sandflies for transmission experiments.

When research on the problem of transmission of kala-azar was renewed this year the possibility of feeding *P. argentipes* on food other than blood was again investigated, and it was found that these insects could be kept alive for quite long periods by feeding them on raisins, in much the same manner as mosquitoes.

The method employed was as follows:—

*Method of feeding flies.*—On the third day after a blood meal on a kala-azar patient the flies are placed in a globular lamp chimney, which is closed at one end with a piece of muslin and plugged at the other with cotton-wool. In the centre of the cotton-wool plug is inserted a specimen tube, about three-quarters to seven-eighths of an inch in diameter, filled almost to the top with cotton-wool, with a shallow cavity to contain the raisins. The rim of the tube was adjusted very slightly above the wool of the plug. The raisins were prepared by washing them in running water for about half an hour and then scalding in boiling water for a minute. Before the flies are introduced into the chimney so prepared, the cotton-wool plug is moistened at the periphery only. Quite a large proportion of the flies oviposit on the moistened portion of the plug and, so long as they are kept without a blood meal, no further development of ova takes place.

The raisins require to be changed every day as the temperature and humidity at which it is necessary to keep these flies cause a rapid growth of moulds on the raisins in a little over 24 hours and sometimes in less.

Instead of the chimney a small muslin cage has been found to be as suitable or better for housing the flies, as the survival rate has very often been found to be greater in cages than in chimneys at the end of a ten-day period; but we have reason to believe that flagellate infections develop better in flies kept in chimneys, probably because a more constant humidity is obtained in a chimney than in a muslin cage.

In the transmission experiments now being conducted the flies are kept until the tenth day, in the manner described above, before they are offered a second blood meal on an experimental animal. Flies at this age are the equivalent of 4th- or 5th-feed flies kept according to the old method of successive blood meals, and flagellate infections may be assumed to be well advanced. Flies which refuse to feed on one day are replaced in a chimney for a further 24 hours, when many of them are found to be ready to feed. This procedure is followed till the batch is exhausted.

*Intensity of flagellate infections.*—The method employed in the previous experiments aimed at keeping *P. argentipes* as nearly under natural conditions in the matter of food, temperature, and humidity, as was possible in a laboratory, on the assumption that by such means would the best results be obtained. The change therefore to the present method of feeding the flies may seem unnatural and unlikely to yield

satisfactory results; flagellate infections however have been found to develop uninterruptedly in the flies and it may safely be claimed that a larger proportion of flies are found with heavy infections by this method than was seen when they were kept on successive blood meals. It is not possible to produce any figures in support of this contention as no record of the intensity of infections in flies was kept previously and it was not possible to maintain a parallel series on blood meals on this occasion. However, the senior author, who has dissected very large numbers of sandflies fed on repeated blood meals in past experimental work, and has also dissected all the flies in this series is of the opinion that in this series the infections are infinitely heavier.

Whether sandflies take any food other than blood under natural conditions is not known, but the fact that *P. argentipes* are most prevalent under rural conditions where there are greater opportunities for imbibing fruit and plant juices, practically throughout the year, is in favour of such a possibility.

*Infectivity of flagellates.*—A test of the infectivity of flagellates from sandflies fed on raisins has been made by inoculating mice both intraperitoneally and subcutaneously with such flagellates. It is hoped to sacrifice these animals in the near future, and the rate and intensity of infection in them will serve as an indication of the results to be expected from the feeding experiments with the flies.

*'Blocked flies'.*—Infected flies that had been fed in the interval by the method described above were on the tenth day given an opportunity to feed on an uninfected animal, by a method that has been used for many years in these experiments, namely, by inverting a test-tube containing one or more flies over the shaved abdomen of the animal. The laboratory attendant holds the tube in position and can observe the whole procedure. A laboratory attendant who had had considerable previous experience noted that certain flies, after puncturing the skin of the animal, were making persistent but futile efforts to obtain a blood meal. As this phenomenon was new to the senior writer also, we decided to investigate it further.

The separation and examination of flies reported to have made persistent efforts to obtain a blood meal without succeeding in doing so, revealed the fact that they were almost invariably heavily infected individuals. These flies were dissected and in certain instances when the head capsules of some of them had been successfully removed it was seen that the proventricular fold was almost completely obliterated and the oesophagus greatly distended with flagellates; on more than one occasion also when recently-dead flies were dissected, flagellates were seen escaping from the anterior end of the pharynx when its attachment to the buccal cavity was severed. These features

have however also been observed in the dissection of flies that showed no signs of obstruction, but not to such a marked extent.

The condition was therefore regarded as one of 'blocking' and similar to that occurring in fleas infected with *Pasteurella pestis*.

'Blocking' in sandflies may be partial or complete. In the partially blocked flies a very small quantity of blood may be seen with the naked eye, but more often the aid of a lens is required to detect this minute quantity seen as a pink discoloration across the thorax of the fly. No blood can be seen in the abdomen. In the completely blocked fly no evidence of blood can be detected with a lens and in such flies no blood is seen in the midgut at dissection.

During August and September, 58 flies were labelled 'blocked' and separated for special examination. The dissection of these flies as they died gave the following results:—

Heavily infected with flagellates ..	49
Negative, no flagellates seen ..	2
Fly decomposed, no result possible ..	7

Once a fly is 'blocked' it is unable to feed again, though when given further opportunities it makes attempts to do so. However, amongst the flies that are placed to feed on the experimental animals on the tenth day, there are both infected and uninfected that take a full meal; these flies are given further 'transmitting' feeds when the previous meal is digested.

The condition of blocking has been observed only among the flies being offered a second blood meal, and not amongst those which are being given third, fourth and subsequent feeds, although among them heavily infected individuals have been found on dissection. If blocking was the result of a progressive multiplication of flagellates exclusively, it should have been encountered oftener (or at least in a few instances) in flies at the fourth or fifth feed, as they had had from two to six days longer for the flagellates to develop. That this is not the case is suggestive that some, at present unknown, factor is necessary in addition to a heavy flagellate infection to produce the phenomenon, or that some factor which prevents blocking is in operation when sandflies are fed on successive blood meals.

The inability of the flies to obtain blood after piercing the skin of an animal is, we think, due to the enormous number of flagellates in the oesophagus rather than in the pharynx or anterior end of the midgut, as described by Shortt, Barraud and Craighead (1926) in a fly of which they cut sections.

*Significance of 'blocked' flies.*—It is suggested that blocked flies are more likely to transmit infection than the ordinarily infected fly, as in their vigorous attempts to satisfy their hunger they are likely to cause the detachment of flagellates from the 'block' which would easily find their way from thence into the wound; more

(Continued at foot of next column)

## THE VENOM OF INDIAN COBRA (*NAJA NAJA*) IN CERTAIN PAINFUL CONDITIONS

By R. N. CHOPRA, C.I.E., M.A., M.D., Sc.D. (Cantab.),  
F.R.C.P. (Lond.)

BREVET-COLONEL, I.M.S. (Retd.)

and

J. S. CHOWHAN, M.B., B.S.

CAPTAIN, A.I.R.O.

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DURING the past few years a great deal of interest has been taken in the use of snake venoms in medical treatment. The results obtained in a series of cases treated in the Carmichael Hospital and School of Tropical Medicine, Calcutta, have been reported previously by the present authors (Chopra and Chowhan, 1937). Since then, the opportunity for treating a large number of patients suffering from pains of varying origin has arisen and, out of these, 65 representative cases have been selected and discussed in this paper.

Snake venoms have been shown to consist of a number of active principles responsible for their clinical effects. The neurotoxin principle, though present in all snake venoms, has been shown to preponderate in the venom of the Indian cobra. This toxin has a selective action on nerve tissue and is responsible for the various clinical uses for which cobra venom is advocated. Micheel and Jung (1936) separated the neurotoxin from cobra venom by ultra filtration and passage through a cellophane thimble, and precipitation. Neurotoxin, in the opinion of these authors, appears to be akin to proteins, although its molecular weight was estimated to be as low as 2,500 to 4,000.

Ganguly and Malkana (1936) reported that all the venoms are compounds of the elements, carbon, hydrogen, nitrogen, sulphur and oxygen

(Continued from previous column)

transmission may thus be expected from 'blocked' flies than from others which, though heavily infected, do not exhibit this particular phenomenon.

In conclusion we take this opportunity to express our thanks to Mr. J. A. Dey for drawing our attention to this condition.

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in addition to phosphorus. The protein constituent of the venoms consists of albumin and globulin as coagulable proteins, and primary and secondary proteoses as incoagulable proteins. The different fractions of proteins can be separated by saturation with ammonium sulphate and represent the total proteins and contain the full toxicity as gauged by the effect on pigeons by the method used for testing neurotoxins. Tetsch and Wolff (1936) undertook chemical analysis and biological tests of different snake venoms. According to these authors the chemical composition of these venoms is as follows :—

TABLE I  
Chemical analysis of different types of venom

Name of venoms	PERCENTAGE				Toxicity per gram of mice
	Nitrogen	Carbon	Hydrogen	Sulphur	
Bee venoms ..	13.6	43.6	7.1	2.6	6-10 mg
<i>Crotalus terrificus</i> ..	14.7	44.9	6.6	3.6	0.7 "
Cobra (species?) ..	14.7	45.2	7.0	5.5	0.12 "

A perusal of these figures will show that cobra venom is the most toxic and probably its toxicity is dependent upon its high sulphur content. Since neurotoxin is the chief active element in cobra venom it is probable that the therapeutic effects of neurotoxin may be due to its sulphur content. Ghosh, De and Bhattacharjee (1937) have succeeded in separating neurotoxin from cobra and Russell's viper venoms in a purified state and have been able to concentrate it to about 10 to 15 times of its potency in the venom. This purification and concentration of neurotoxin of cobra venom has a very important bearing on the preparation of cobra venom for therapeutic purposes. It is now possible to use neurotoxin in various nerve and other complaints in place of colloidal solution of crude cobra venom which is being used at present. It however remains to be decided if purified neurotoxin or cobra venom, as it exists in nature, is the more effective of the two.

Oh (1936) tested the action of Formosan snake venoms on the motor and sensory nerve endings and on the pain centre. For the former he used Santessou-Osaki method with frogs as experimental animals and for its effect on the pain centre he employed the Okushima method of injecting the venom subcutaneously in the back of mice and testing the pain responses by pricks on the tail. This author observed that the venom of *T. gramineus* and *Naja atra* paralysed the sensory nerve endings of the frog more rapidly than the venoms of *T. micro*

*squamatus*, *Ancistrodon acutus* and *Bungarus multicinctus*. In the case of paralysis of motor nerve endings, *Naja atra* had the most rapid action compared with other venoms. The pain centre in mice is markedly depressed with 0.000,1 mg. and obviously with 0.000,05 mg. of venom of *Naja atra* per gramme weight of mouse and markedly with 0.003 mg., and distinctly with 0.000,5 mg. of *B. multicinctus* venom per gramme body-weight of mouse. Kellaway (1937) reported that all the Australian snake venoms along with the Indian cobra have a paralytic action *in vitro* on the sensory nerve endings in frogs (*Hyla aurea*) though this action was less powerful than on the motor nerve endings. Cicardo (1935) reported that cobra venom increases the rheobase and chronaxie of the motor nerves before curarization. Muscle chronaxie may also be increased. The changes in sensory nerves may take place before those in the peripheral motor nerves. Macht (1935) demonstrated the analgesic effect of cobra venom in man and guinea-pigs. After subcutaneous and intramuscular injections, the susceptibility to pain caused by an electric current was greatly diminished and lasted for several hours. This author (Macht, 1938) further summarizes his various observations on the action of cobra venom on the nervous system. He believes that, in therapeutic doses, cobra venom affects neither the sensory nor the motor nerve endings nor the ascending nor descending fibres of the peripheral nervous system. The analgesia produced is central in origin and closely resembles that produced by morphine. In experiments on normal human beings, injections of cobra venom either markedly increased the resistance to pain or heightened the sensory threshold. In experiments on mice, rats, and guinea-pigs, it was found that cobra venom injections antagonized the action of certain convulsant drugs, such as camphor, metrazol and picrotoxin. This anti-convulsant and analgesic action of cobra venom led to the discovery of its usefulness in paralysis agitans and Parkinsonian syndrome. Fabbri (1938) also believes that the action of cobra venom is through the central nervous system. He treated 25 cases of sciatica, polyneuritis, lumbago, intercostal neuralgia, trigeminal neuralgia and the gastric crisis of locomotor ataxia. The initial dose in every case was 0.04 mg. injected intramuscularly and repeated 2 to 3 times a week. The relief usually followed after the fifth or sixth dose. Some of these cases who, previous to this treatment, required large doses of morphine to suppress their pain, were now free from their symptoms. Occasionally local swelling, pain, redness and pyrexia occurred at the site of injection. Local reactions such as skin eruptions and glandular enlargements lasted for one to two days after the injection. These symptoms usually appeared after such a large dose as 0.1 mg. and could be avoided by deep intramuscular injections. Laignel-Lavastine, Warmser and Koressios



(1934) believe that the action of cobra venom is on the peripheral vasomotor nerves.

Calmette has shown that cobra venom has a special affinity for phosphatic elements, especially lecithin of nerve cells, producing a compound which suppresses the sensibility to pain without, however, interfering with the conductivity of motor nerves.

Recently evidence has been advanced to show that most if not all motor nerves, on stimulation, liberate acetylcholine at their endings and that this substance and not the nerve itself carries the impulse across the synapse to the end-organs. This acetylcholine is rapidly destroyed in the blood by the presence of a specific choline esterase in the plasma. If, therefore, acetylcholine is prevented from reaching the receptor end-organ by its destruction through choline esterase, apparently the impulse will not pass across the end-organs to the responsive tissues. Iyengar, Sehra, Mukerji and Chopra (1938) reported the presence of appreciable amounts of esterase in cobra venom itself. This finding offers a new and plausible explanation regarding the pain-relieving property of cobra venom. Choline esterase in cobra venom will supplement the activity of choline esterase in blood, will help in destroying the acetylcholine at the terminal ends of these nerves and will thus prevent the transmission of impulses from the nerves to the tissues and *vice versa*. It will in this way cut off the extraordinary and exaggerated sensation or impulses passing between the nerve and the tissue.

#### *Cobra venom in different types of pain*

Kirschen (1936) reported on the analgesic action of cobra venom in neuritis in man and also in spontaneous and transplanted carcinoma in mice. The pain was reduced with small doses. In cases where the improvement was felt, the same dose was repeated, and the interval of injection was lengthened. The dose was increased if no improvement followed after the fourth or fifth injection. He concluded that though cobra venom has no specific effect in carcinoma in man, it has, however, a decided analgesic effect which is of great significance. He treated seven cases of neuritis of which two were severe sciatica. He used a colloidal solution of standardized cobra venom, free from bacteria, hæmorrhagins and hæmolysins, supplied by the Dumatras Laboratory of Paris.

Brünner-Ornstein (1937) recorded gratifying results in obstinate cases of trigeminal neuralgia; relief was speedily obtained in half an hour. Of the 14 cases of severe neuralgia, six had been suffering from pain for three to four months and were considerably relieved after the treatment. In a few cases he used Crotaline venom, but this venom did not give encouraging results. Burgess Barnett in a personal communication informed him that he had obtained excellent results in tabetic crises.

Rottmann (1937) reported on 10 cases of tabes from Vienna university clinics all of whom improved remarkably after treatment. He used cobra venom (species not mentioned) in 5 c.cm. ampoules containing 200 mouse units. Starting with 10 mouse units as an initial dose he increased it by 25 and 30 units at intervals of 7 to 10 days and went up to 60 mouse units. He believes that the good results obtained were due to its action on the specific granulation processes. He is also of opinion that the venom is not of much use in meralgia paræsthetica, amputation neuralgia, and herpes zoster, though it has been found beneficial in cases of herpes simplex. Bullrich (1937) obtained good results in six cases of angina pectoris, and arterio-sclerosis with attacks of angina, syphilitic aortitis with aortic insufficiency due to coronary sclerosis. Intravenous injections were given every third day, beginning with a dose of 0.25 c.cm. followed by 0.5, 0.75 and 1 c.cm. The number of injections depended upon the severity of the case and the reaction produced. The preparation corresponded to the standard of Calmette and Taguet, 0.1 mg. representing 5 m.u. Seiler (1936) used cobra venom in cases of severe sciatica and pains in the legs due to arterio-sclerosis, bronchial carcinoma and cancer of the prostate with pain in the legs. He entirely failed to confirm the claims made by other workers on the efficacy of cobra venom as an analgesic, and added that this failure might be due to impurity of the venom used by him.

#### THE PREPARATION AND USES OF COBRA VENOM

Injectable venom, as prepared by the present authors in the School of Tropical Medicine, is a colloidal solution of fresh venom of the Indian cobra (*Naja naja*) obtained through the courtesy of the Director of the Haffkine Institute, Bombay. The solution was prepared by dissolving the venom in sterilized normal saline solution in concentration of 1-10,000, 0.25 per cent of carbolic acid being added. Its sterility was tested for types of bacteria and particularly those of gas gangrene and tetanus groups. The solution was packed in 10 c.cm. rubber-capped vaccine bottles and stored in refrigerators. The preparation was standardized in strength of 10 mouse units (m.u.) per c.cm. It was observed that after stocking it for a few months, a thick flaky deposit settled at the bottom of the containers. The supernatant fluid was tested again for sterility and toxicity. It was shown that the venom solution after stocking for six to ten months still represented about eight mouse units per c.cm., and was free from bacterial contamination. Bagnasco, Aguilar and Garzoli (1938) reported that the cobra venom solution used by them for therapeutic purposes deteriorated after 6 to 8 months.

*Contra-indications.*—Before starting cobra venom injections the conditions of the excretory organs should be carefully investigated. Bagnasco and his associates (1938) observed



that the patients with cardiac disturbances, aortitis, cardiac insufficiency, etc., did not give satisfactory response. Patients failing to improve after 2 to 3 injections were regarded by them as refractory cases. The treatment, in their opinion, is incompatible with administration of iodine, gold and silver salts and radioactive substances.

The present authors have observed remarkable sensitiveness in a few cases only. The symptoms as observed by Taguet and Monaelsser were sleepiness, restlessness, acute inflammation at the site of injection, respiratory difficulty, nausea, diarrhoea or vomiting, and palpitations. Such marked symptoms were not seen by the present authors. Local sensitiveness in the form of redness and swelling at the site of injection and sometimes even blistering were observed, the latter condition occurring usually with Russell's viper venom injections. In some cases the original symptoms were temporarily exaggerated after the injection of cobra venom, but this was regarded as a symptom of reaction. The present authors as a rule started with a very small initial dose, particularly in the case of women, children and debilitated patients, such as those suffering from cachexia of malignant disease. In such cases one-tenth of a mouse unit was the first dose. Later the dose was increased, with due regard to the response given by the patient. Resistant cases, or cases which showed no improvement with 4 to 6 doses, were given vitamin B<sub>1</sub> with good results.

Cobra venom has been extensively used by the authors in all types of pain. Gass (1938) and Chowhan and Chopra (1938) reported on the use of cobra venom in pains of nerve leprosy. The series of cases discussed in this paper were in-patients both in the Carmichael Hospital for Tropical Diseases and in the out-patient department of the Calcutta School of Tropical Medicine (see table IV). Usually the injections were given intramuscularly, twice or thrice weekly, in doses ranging from one to twenty mouse units. In some cases, where prolonged treatment was required or ordinary doses did no good, strong solutions containing a hundred mouse units per c.cm. were given by the intradermic route. In some cases, vitamin B<sub>1</sub> was also given in addition to cobra venom. The cases are grouped as:—

(a) Those who showed marked improvement, and were for all practical purposes cured and free from their complaints.

(b) Those in whom relief of symptoms was definitely evident, and according to the patients' own version 50 per cent of the complaints were relieved.

(c) Those in whom the benefit was slight, doubtful or *nil*.

The patients treated in the hospital were first thoroughly investigated in order to find out the

cause of the pains. Their diseases can be grouped as follows:—

TABLE II

Neuritis, neuralgia, diabetic neuritis, post-filarial neuritis, etc. ..	26	Orchitis and funiculitis ..	2
Sciatica ..	13	Cerebral diplegia ..	2
Lumbago and fibromyositis ..	4	Paraplegia ..	3
Osteochondroma and arthritis ..	8	Progressive muscular atrophy and tabes dorsalis ..	1
Paræsthesia ..	1	Habit spasms ..	1
Nerve leprosy ..	2	Chronic headache ..	1
		Trigeminal neuralgia with tic ..	1
		TOTAL ..	65

The total number of cases treated and the percentage in each group are shown in table III.

TABLE III

*Effect of cobra venom treatment on patients grouped according to the degree of relief obtained*

	Number of cases	Percentage
(A) Marked relief ..	23	35.4
(B) Definite relief ..	23	35.4
(C) Slight relief ..	9	13.80
(D) Doubtful or no relief ..	10	15.40
TOTAL ..	65	

In order to economize in space, only representative cases in each group are quoted (table IV).

It will be seen that out of 65 patients 35.4 per cent were reported to have been cured or to have had marked relief. In these cases 5 to 15 injections of cobra venom were administered. The maximum dose of the venom reached was 20 m.u. Usually the initial relief was reported after the third or fourth injection.

In two cases injections of vitamin B<sub>1</sub>, or novalgin, were given. The relief was accelerated by addition of vitamin B<sub>1</sub> to cobra venom therapy. Stevenson (1938) has already reported that vitamin B<sub>1</sub> is very useful in neuritis. He used it empirically and found that, of cases of sciatica and neuritis, about 33 per cent were almost cured. In another 35.4 per cent there was also definite relief (*i.e.*, in about 50 per cent there was relief of symptoms). Taking both these batches together it is observed that about 70 per cent of patients are markedly relieved of their symptoms.

Intradermal injections were tried in cases where doses of more than 20 m.u. were to be used. This method seemed to possess no particular advantage over the intramuscular route: In 13.8 per cent there was only slight relief and usually prolonged treatment was required; most of these cases were suffering

TABLE IV  
*Different types of painful conditions treated with injections of cobra venom*

Number	Age, caste and sex	Symptoms	Diagnosis	Present treatment (mouse units)	Effect
A.* 1	35, H., M.	Pain left side of head, neck, arm and shoulder six years, tremors of tongue, neck and hands.	Progressive muscular atrophy.	5, 6, 8, 10, 12, 10, 12.	No pain, slight tingling left arm.
2	49, E., M.	Pain left chest, left shoulder, arm, 1st and 2nd fingers. Numbness in finger tips and finger nails. One year.	Brachial neuralgia	2, 4, 6, 8, 10	No more pain, feels much better.
3	21, H., M.	Pain in lumbosacral region constant and dragging in type, duration two years. X-ray examination showed a growth of the ischial tuberosity.	Osteochondroma of ischial tuberosity.	2, 4, 6, 6, 8, 9, 10, 10, 10, 10, 10—two months later 50, 70 due to recurrence of pain.	No pain after 12 injections, two months later slight pain relieved by two large injections. Has not been seen again.
4	46, E., M.	Vague pain in thoracic spine, not elicited by tapping on the head or the spine. Pain in calf muscles, headache and burning sensation in skin and the trunk, shifting in character, hyperæsthesia left calf and foot, less on the right side.	Paræsthesia	1, 2, 4, 4, 5, 5, 8, 10.	Ninety per cent relief. No report for two years.
5	25, E., M.	Spasmodic attacks of pain in the sternomastoid for 1½ years, six months ago temporo-mandibular joint stiff, filariasis in 1930.	Temporo-mandibular arthralgia.	1, 2, 3, 4, 6, 8, 8, 8, 10, 10, 10.	Marked relief.
6	60, A.-I., F.	Hemicrania left side three years; pain left side of body one year, at present pain in right thigh shooting downwards and vague pain all over the body and left knee.	Peripheral neuritis and teno-synovitis.	2, 4, 6, 8, 8, 4	No more pain.
7	48, H., F.	Epidemic dropsy 1½ years. Pain hips, shoulders and scapular region on both sides, tremors of hands and arms of paralysis agitans type.	Neuritis due to post-epidemic dropsy and Parkinsonian syndrome.	0, 5, 1, 2, 4, 6, 8	Considerable relief, no return of pain.
B.* 1	30, H., M.	Tingling sensation, urticaria hands and feet. Epidemic dropsy one year.	Neuritis and urticaria.	2, 4, 4, 6, 8, 8, 10, 15 (intra-dermal injections).	Definite relief.
2	30, H., M.	Paraplegia six months, started as pain in thoracic region radiating downwards followed by paralysis of both legs.	Paraplegia	2, 4, 6, 8, 10	Definite relief.
3	40, H., M.	Severe pain along the left limb for three years, worse for three months.	Sciatica	3, 5, 6, 8, 10, 10, 10, 10, 8, 10.	Definite relief.
4	33, H., M.	Pain in testicles and spermatic cord and pulling sensation in scrotum 15 years. Hydrocele operated on a year ago; no improvement, impotent.	Orchitis and funiculitis.	2, 4, 6, 8, 10, 10, 10 (vitamin B <sub>1</sub> and C injections along with cobra venom 10, 10, 10).	Definite relief of pain.
5	40, H., M.	Hard immovable growth left thigh 3" × 7" × 2½", hard and smooth; pain constant, severe at night, duration two years. Pain radiates downwards.	Osteoperiostitis	0.75, 0.75, 2, 4, 6	Some relief. Treatment discontinued.

\* See table III.

TABLE IV—concl'd.

Number	Age, caste and sex	Symptoms	Diagnosis	Present treatment (mouse units)	Effect
6	30, H., M.	Stiffness of neck muscles and back, gonorrhœa 12 years ago, spermatorrhœa, no pains in joints, pyorrhœa alveolaris.	Fibromyositis (gonorrhœal).	2, 2, 6, 8, 10, 10, 10, 15.	Marked relief.
7	51, H., M.	Pain left thigh and legs two months, relieved when he sits. Pain worse on walking.	Sciatica	5, 7, 10, 10, 10, 10, 10.	Fifty per cent relief, did not return for further treatment.
C. 1	35, H., M.	Snake bite six months ago, neuritis two days later, no other toxic symptoms of venom.	Neuritis after snake-bite.	2, 4, 6, 6	Slight relief.
2	20, M., M.	Pain left buttock and leg and foot, tingling left foot.	Sciatica	2, 4, 6, 6, 8, 10, 10, 10, 15, 10, 20, 50, 50, 50, 50, 50, 50.	Slight relief after prolonged treatment.
D. 1	40, H., M.	Pain in left buttock, radiates to left thigh and foot.	Sciatica	1, 3, 3, 5, 7, 5, 5, 10. No relief. Advised veramon 5, 6, 8, 10.	Little or no relief.
2	18, H., M.	Spastic paralysis both legs since childhood, contracture deformity upper limb.	Cerebral diplegia	1, 2, 4, 6, 6, 8, 10, 10, 12.	No relief.
3	51, M., M.	Pain shoulders and limbs; hands and feet, wrist bone swollen, syphilis 22 years.	Arthritis (venereal)	2, 4, 6, 8, 8, 8	No relief.
4	20, H., M.	Measles February 1936, persistent headache, could not carry on his college studies. Pain is constant, sometimes so severe that he cannot open his eyes or read; fainting fits and clonic spasms.	Chronic headache	He had <i>Rauwolfia serpentina</i> and bromides, no relief. 2, 4, 6, 8, 10, 10, 10.	No relief. Spasms stopped.
5	47, H., M.	Left trigeminal neuralgia 3½ years without any definite cause. Various injections given, slight relief. Started after removal of his teeth. Wassermann reaction negative.	Trigeminal neuralgia	5, 8, 10, 15, vitamin B <sub>1</sub> and 15, 15, stopped.	Temporary or doubtful relief.

from sciatica and lumbago. In sciatica, relief is not marked since the pain may be due to pressure on the nerve, or fibrous adhesions in the sciatic notch may be constantly irritating the nerve. In 15.4 per cent of patients there was no relief at all. One patient of this group was suffering from habit spasms and the other from *tic douloureux*; the latter was finally shown after x-ray examination to be due to an abscess in an alveolar socket in the lower jaw. In cases of chronic headache, improvement was not marked.

**Conclusion.**—Cobra venom plays a definite part in relieving pain of an indefinite nature in a large number of patients. Its action is often slow, but in many cases certain and lasting. It may be used with impunity in chronic pains of nervous and muscular origin, arthritis and in inoperable malignant disease, with beneficial results. Purified neurotoxin is now being prepared for trial to determine if it is more

effective than the whole cobra venom which is being used at present.

**Summary.**—(1) Cobra venom has been tried in various types of vague and indeterminate painful conditions.

(2) In about 70 per cent of cases there was marked and considerable relief of pain, and in about 30 per cent of the cases the relief was doubtful or indefinite.

(3) The pain disappears slowly but the effect is lasting.

(4) No untoward symptoms were produced by the injections.

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(Continued at foot of opposite page)

# THE TREATMENT OF CARBUNCLE IN THE OUT-PATIENT DEPARTMENT

By CHITTA RANJAN DUTT, M.B.

Howrah

THE introduction of autohæmotherapy in the treatment of carbuncle has given very good results in my hands, much better than the old method of surgical treatment.

The technique consists of injection of the patient's own citrated blood, the amount depending on the area affected, usually about 10 to 20 c.cm. each time, starting about half an inch within the extreme margin of induration and injecting gradually as the needle is pushed towards the centre of the carbuncle till some blood wells out of the small openings over the carbuncle. About four lines are so treated each time. The patient gets about two to four such courses. In addition ordinary boric or saturated magnesium sulphate compress is applied to keep the part free from the foul pus discharge.

This method of treatment is usually done on patients who can be kept under control in the indoor wards or in private houses. But it can be carried out on out-patients who probably visit twice or thrice a week, and in this fact the interest of this article lies.

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This method has been tried with very good results on many patients who consented to be treated as out-patients. After one injection the induration becomes less, the swelling localized and discharge of pus free and thin and not like thick sloughs. The pain is much less or disappears entirely and one can sleep well. After two or three injections the whole part becomes covered with red granulations underneath and in most cases the overlying skin is not dead. It was found that this method certainly cuts short spread of the disease and also lessens very much the period of convalescence.

Carbuncles of various sizes from 10 inches in diameter to 2 inches in diameter were treated. Carbuncles in various situations including one on the face were also taken up in the series. The results were uniformly good and there was no untoward effect because of the patients being treated as out-patients.

*Case 1.*—Adult male, age 60. Carbuncle situated in the dorso-lumbar region on the right side of the spine. At his first visit on 6th July, 1937, the indurated area was 5½ by 3½ inches, there was burning sensation and the patient could not sleep at night. Temperature 99°F., pulse 88, respiration 24. Urine—sugar and albumin nil.

Five injections were given, the first being performed on the day of his first visit. After the first injection pain much abated and after the second it disappeared almost completely and temperature came down to normal and pulse/respiration 80/20. After the 4th injection, slough separated completely and the skin over the area was healthy and the area of induration was reduced to 3½ by 2½ inches. Saturated magnesium sulphate compress was applied throughout the course of treatment. On 20th July only two small superficial ulcers ¼ inch in diameter were left and the patient was advised to dress with unguentum borovaseline. An alkaline mixture with potassium bromide was administered throughout the course.

*Case 2.*—Adult male, age 52. Carbuncle situated on the right buttock. At his first visit on 19th August, 1937, the indurated area was 5 inches in diameter, there was severe pain and the patient had three sleepless nights. Urine—sugar and albumin nil.

Two injections of 10 c.cm. each were given. After the first injection only slight pain was felt and after the 2nd injection on 25th August the area of induration was 2 inches in diameter. Saturated magnesium sulphate compress was applied and at first potassium bromide and later mistura ferri et strychninae 5i, t.d.s., were administered. Tiny ulcers were left after the 2nd injection, which were dressed with unguentum borovaseline.

*Case 3.*—Adult male, age 40. Carbuncle situated over the occipital region. At his first visit on 25th September, 1937, the indurated area was 5 inches in diameter extending from external occipital protuberance to 7th cervical vertebra and from one mastoid to the other mastoid region. There was burning sensation and the patient had no sleep for last three or four nights. Urine—sugar and albumin nil.

Two injections each of 10 c.cm. were given at an interval of 48 hours. After the first injection the pain markedly diminished and the patient could sleep at night. Magnesium sulphate compress was used and magnesium sulphate and glycerine paste was applied over the indurated area. The patient was advised pulv. A. P. C. on the day of his first visit to relieve the pain. On 10th October two superficial ulcers each ½ inch in diameter were left and the skin over the area was healthy.

*Case 4.*—Adult male, age 49. Carbuncle situated on the left cheek. At his first visit on 7th October, 1937, the indurated area was 2½ by 2 inches in diameter.

There was burning sensation. No sleep at night. Urine—sugar and albumin *nil*.

One injection of 6 c.cm. was given on 7th October and on 13th the overlying slough completely separated. Healthy granulating surface appeared. Magnesium sulphate was used as a compress throughout the course of treatment and potassium bromide mixture  $\bar{5}$ i, *t.d.s.*, was administered. After the first injection the pain almost completely disappeared. Subsequently the wound surface was dressed with unguentum borovaseline.

**Case 5.**—Adult female, age 50. Carbuncle situated on the middle of the back on the left side. At her first visit on 28th June, 1937, the indurated area was  $3\frac{1}{2}$  inches in diameter. The condition was sloughing and there was severe burning pain and fever. Urine—sugar and albumin *nil*.

Four injections were given the first being performed on the day of her first visit. When she came to the outdoor after the first injection, she said that the pain had disappeared completely. When she came on the 4th day after the first injection she complained of slight pain when the 2nd injection was given. After that, she never complained of pain. Magnesium sulphate compress was applied throughout the course and potassium bromide mixture  $\bar{5}$ i, *t.d.s.*, was administered. After the 4th injection, the slough completely separated and the ulcer considerably reduced in size. Patient went home on 13th July on her own initiative and when she again came to the outdoor on 22nd only a scar  $\frac{1}{2}$  inch in length was left.



Case 6.—Before treatment.

**Case 6** (an indoor patient at the Howrah General Hospital).—Male, age 60. Appearance on 3rd May, 1939, when the first photograph was taken. Carbuncular area  $5\frac{1}{2}$  inches in diameter. Not much induration around. Multiple openings covered with thick sloughs. No sleep for five nights. Urine—sugar and albumin *nil*. Blood sugar—112 mgm. per 100 c.cm. Ten c.cm. blood injected in the upper quadrant in three situations. Pain much diminished 24 hours after the injection and patient had a good sleep at night. Magnesium sulphate compress thrice daily. Patient could not keep his head erect.

On 9th May the necrosed area had diminished to 2 inches in diameter with complete separation of

(Continued at foot of next column)

## OBSERVATIONS ON THE PATHOLOGY AND THERAPY OF THE SO-CALLED FRONTIER SORE

(SECOND COMMUNICATION)

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**Introduction.**—In an earlier paper (1939) we drew certain conclusions about the clinical complex of so-called frontier sore, the chronic ulcer which is so common in N. W. India, using as material 88 cases. These conclusions were:

(1) Frontier sore is a clinical entity. Only laboratory examination reveals various aetiological groups, where history and clinical observation have failed. The aetiological groups are

(Continued from previous column)

sloughs. Twenty-four hours after that granulation appeared. Almost no pain. Major part of the skin over the peripheral part of the carbuncular area tending to become normal. When granulation appeared compress stopped and unguentum borovaseline applied.



Case 6.—After treatment.

Patient's condition was very low on admission. Pulse soft; patient—anaemic; temperature— $100^{\circ}\text{F}$ ., so was given an alkaline and bromide mixture. Fifty cubic centimetres of 25 per cent glucose intravenously twice daily. Camphor in ether 1 c.cm. four hourly was administered when pain and temperature abated. *Mistura ferri et strychninae*  $\bar{5}$ i, *t.d.s.*, given. The patient had an attack of benign tertian malaria and quinine sulphate was administered. Temperature came down to normal, the local condition much improved and the patient was discharged to attend the outdoor for dressing.



mainly characterized by Leishman-Donovan bodies, Klebs-Loeffler bacillus and, in about 89 per cent of the total, by non-specific common pyogenic organisms, mainly *Staphylococcus aureus*.

(2) The exact microscopic diagnosis permits specific treatment for each case according to the organism revealed. For the big group of sores with common pyogenic organisms and secondary invaders, compounds containing sulphonamide proved to be of efficacy in local application.

*Subject of this study.*—It was desirable to find further evidence for these conclusions. The present study is concerned with an attempt to clarify the uncertainty about the history of the frontier sore. We wanted further to confirm in another-locality the previous statements, namely that the frontier sore is an affection in which mainly the common pyogenic organisms are found, and that sores which reveal Leishman-Donovan bodies form only a minor group. Further, we wanted to obtain more data about the efficacy of the local sulphonamide treatment, and to improve it if possible.

*Method.*—In the middle of December 1938 we were asked to examine a batch of 58 men who had returned to their station after having served in Tonk (South Waziristan) during the hot weather of 1938. They all belonged to the same unit. Twenty cases were selected for observation, who had shown no response to routine treatment. The others were asked about the duration of their disease from the beginning to the present state of relative improvement. Histories were taken in all, with special emphasis on diet.

The 20 selected cases were examined as described in the first article. For technical reasons only a small number of bacteriological examinations could be undertaken. These, however, are representative. The examination for Leishman-Donovan bodies was done in each case. In some of them a parallel examination was carried out by the district laboratory, Peshawar, and by us in Rawalpindi. There were no differences in the two independent series of examinations.

Treatment was carried out entirely by the staff of the military hospital where the patients attended, and the results were put down in the previously mentioned forms. We re-visited the out-patient department only once seven days after treatment was begun. The data collected in the first inquiry and examination of the 56 cases, at the second intermediate inspection seven days after the beginning of treatment, and the hospital report after completed cure, is the source of the material for this study.

### Results

*History.*—Differing from our previous experience, the enquiry into the history was successful. All 58 men stated that the sore, occurring after an insect bite, perhaps a mosquito, began to develop into a small boil and from that into the sore. All the men had acquired the condition

between 15th February and 15th November, 1938, when in Tonk. Out of 80 men in this unit 58 were affected. Another unit which had been at Tonk during the hot weather of 1937 had a great number of cases with long total or partial disablement. We have had the opportunity of seeing a number of these 1937 cases and are convinced that, though we could not collect exact figures, they represented the same affection. In a group of men of the same unit, who had been stationed at Tonk between 25th December, 1937 and 15th February, 1938, only one case occurred who did not develop these sores until November, and he had been out of the station. A further group, which was stationed during the hot weather of 1938 at Bannu (not far from Tonk), had only one case of frontier sore.

*Duration.*—The duration of the disease under routine treatment, that is, with simple ointment, aeriflavin dressings, hot fomentations, scraping or occasionally emetine injections, varied between 3 weeks and 8 months, the average being 4½ months. The duration of the 20 cases, who came subsequently under closer examination and treatment, varied between 1½ and 5 months, the average being 3½ months. This indicates once more the extreme chronicity of the frontier sore and the unsatisfactory state of routine treatment now employed.

*Diet.*—The food which the affected men received was mixed and varied. There was no evidence of any possible food deficiency. The men were given fresh onions two or three times a week while in Tonk. Meat however had not been available, but was eaten by all in the home station since their return. The use of meat had apparently no influence upon the occurrence of the sores or their reluctance to heal.

*Clinical aspect.*—The healed or almost healed cases show a flat, sometimes depressed, scar. It is frequently depigmented, always soft and indolent. Sometimes a cover of few dry scales is found. Frequently atrophy of the skin is noticed.

The clinical picture of the twenty cases who came subsequently under treatment was as follows:—The sores, single as well as multiple, were situated on the extremities, except for two on back and face. Knees, ankles, elbows, forearm and back of hand are the commonest sites of the condition. In more than half of the cases this type of ulcer, with or without a scab, was found; in the rest of the cases we found an infiltration and hardness, with only small skin destruction through which a little discharge penetrated, which was only in one case purulent. Cyanosis, atrophy, cedema, dry scales are frequently met with. A peculiarity of this batch of sores was that in eight cases small papules were noticed in the circumference of the ulcer, or they extended over the entire infiltrated area, giving the impression of a lupus-like affection. It has been found that similar papules occur round leishmania sores after their injection with



berberine sulphate, or even without that—after prolonged ointment treatment.

It might be just the expression of a non-specific reaction of the skin to repeated irritation.

**Ætiology.**—Not one of the cases revealed Leishman-Donovan bodies. Six cases were bacteriologically examined. Smears from the surface were taken as well as serum from the indurated base or border of the ulcer, and inoculated on Loeffler medium. Three of the cultures were sterile, in all of which the sores were 'closed'. The 3 others gave a spore-bearing organism of the *Subtilis* group, *Staphylococcus aureus* and a diphtheroid, all of which seem to be secondary invaders. The finding of 3 different organisms along with the same clinical picture and equal response to treatment allows the conclusion that this frontier sore is a non-bacterial infection which must be carried by insects. The findings reported in our first paper fit into this conclusion.

**Treatment.**—For the treatment 20 cases were divided into 3 groups :—

Treatment	Number of patients	Number of applications needed, daily or every other day	REMARKS
Four applications of AS <sub>2</sub> ointment, thereafter 5 per cent prontosil ointment.	10	8	AS <sub>2</sub> was not proving very effective, hence changed to prontosil, all cured.
Five per cent prontosil ointment.	5	6	All but one cured, who improved after ten applications.
Five per cent prontosil ointment + prontosil rubrum gr. 7½, t.d.s.	5	8	All cured. In one case oral treatment was given up, as leucocytes decreased in differential counts from 64 to 48 per cent.

AS<sub>2</sub>, the exact chemical formula of which is not known to us, is according to the manufacturers a compound of the disceptal series, closely related to uleron. Messrs. Bayer inform us that it has given particularly good results in laboratory experiments against virus diseases. Its efficacy has, however, in our particular application been disappointing, as compared with the next treatment.

The 5 per cent ointment with prontosil rubrum or prontosil base (4-sulphonamide-2' 4'-diamino-azobenzol) showed the best results and proved to be an effective and economical treatment for this type of frontier sore. An outstanding case may be given, as representative

of the many dramatic cures we have seen with this treatment :—

**Case.** A follower (water carrier), about 45 years. Total duration four months under routine treatment. General health good. Over lower third of the left tibia, 2 : 2 inches large deep weeping ulcer. At the bottom a few unhealthy granulations. Surrounding skin showed atrophy of dermis.

After four applications of prontosil ointment 5 per cent the ulcer flattened out and became shallow, with no weeping, but healthy granulations in the centre, meanwhile the outer edges were covered with epithelium which grew towards the centre. After six applications complete cure.

The combined oral and local treatment has not shown itself superior to the local treatment alone. The latter has the advantage of being easier, as no control of the blood picture, mainly of the leucocytes, is necessary.

The local application of prontosil is commanding more and more interest. Besides the publications dealing with the local uses of these drugs mentioned in our previous article, we have found now further reports about this method of applying sulphonamide compounds. Recknagel (1935) applied prontosil in big abscesses, locally. Tilling (1936) and Brown (1937) report that empyemas heal rapidly if after aspirating pus from the cavity 5 c.cm. of 2.5 per cent prontosil is instilled. There are reports about the value of prontosil and related compounds in septic throats and urinary, mainly gonorrhoeal, infections, locally employed. The *Deutsche Medizinische Wochenschrift* of 21st January, 1938, gives a general survey of the many local uses of prontosil.

The present communication may contribute to indicate the amazing wide range of usefulness of sulphonamides in fighting infections.

#### Summary

(1) The so-called frontier sore is not a leishmanial infection. There is a certain amount of evidence available that it is a non-bacterial disease carried by an insect.

(2) Prontosil rubrum has again shown itself in local application to be effective. It is superior to AS<sub>2</sub>, a disceptal compound.

#### Acknowledgments

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To Dr. O. Urchs from Bayer Remedies, Bombay, we owe thanks for the generous supply of prontosil, prontosil ointment, and AS<sub>2</sub>.

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## AORTALGIA OR ANGINAL PAIN OF AORTIC ORIGIN

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The syndrome of 'aortalgia' was brought to the attention of the medical profession, for the first time, by Ortnier; he mentioned a few points of distinction between true angina pectoris (Heberden's angina) and aortalgia and considered the two conditions aetiologically and clinically distinct. While regarding angina pectoris as a disease of the coronary arteries and nerves, he attributed aortalgia to an affection of the aortic walls. This view was upheld by Frank and Worms (1926) of Berlin.

Whereas angina pectoris has been recognized for a hundred and fifty years, aortalgia is a new-comer into the field of cardiology. Because of its comparative rarity and the scant attention paid to it by the medical profession, especially in the English-speaking countries, many clinicians are unaware of its very existence.

The following cases of anginal pain, which conform to the clinical description of aortalgia, are sufficiently unusual to warrant publication :

*Case 1.*—A Parsee of about seventy years of age was seen, last year, complaining of difficulty in writing and walking, attacks of giddiness and pains in the chest. The symptoms were progressive and had been noted for about two years.

The pains were anginal in character, in that they came on after exertion, were relieved by rest and nitrites, were confined to the sub-sternal region, and had a tendency to radiate to the left shoulder and elbow. The pains, however, used to last for as long as ten to twenty minutes and were followed by sensations of tingling and numbness in the left upper extremity, for a period of two or more hours. Stroking the surface of the skin with a pointed match-stick revealed areas of hyperalgesia in the left axilla and in the inter-scapular region at the back.

Fluoroscopy showed an 'unfolded aortic arch' with considerable calcification of its walls. The radial and popliteal arteries were tortuous, hard and calcified. The blood pressure was 108/67.

The patient was given a course of Entodon injections in an attempt to prevent further atheroma. He was then put on a mixture containing potassium iodide and nitrites and was asked to report periodically, but has not as yet done so.

*Case 2.*—A Parsee male, aged 69, was examined in November 1939. He complained of attacks of shortness of breath and oppression across the upper part of the chest, at the level of the angle of Louis, on walking or climbing stairs; these attacks, which occasionally come on after a heavy meal or a hot bath, compel him to 'stop at once' or lie down. They were first noticed about the middle of 1937; they are getting more frequent and are easily induced. The pain, which lasts twelve to fifteen minutes, is seldom severe; it is accompanied by a dragging sensation or 'tense feeling' in the chest, shoulder and upper arms; at times, this sensation is confined to one arm and shoulder only (left or right); there is usually a feeling of soreness in the left axilla during the attacks.

There is nothing of note in the patient's past medical or family history.

*On examination.*—He is a short stout individual of the plethoric type and very energetic. He is obviously worried about his condition. The pulse is regular

except for an occasional extra-systole. The systolic blood pressure varies from 120 to 140 and the diastolic from 80 to 95 mm. Hg.

The size of the heart is normal; no murmurs are audible and the aortic second sound is loud and ringing in character.

The electrocardiogram shows some degree of left ventricular hypertrophy. Fluoroscopy shows a dilated aorta (transverse diameter : 7.6 cm.) with a moderate degree of calcification of its walls.

The patient, who is under observation at the present time, is on a mixture containing potassium iodide and sodium nitrite.

*Case 3.*—An Englishman, aged 55, was seen in 1937 in Liverpool. He complained of giddiness and attacks of sub-sternal pain on exertion, each attack lasting for about a quarter of an hour. The pain, which was associated with feelings of tingling, used to spread to both shoulders. The attacks of pain were attended by discomfort in the left axilla with tenderness lasting for several hours after the actual attacks. The pains were located high up behind the sternum and responded but slowly to rest and nitrites.

The man was found to have a rough systolic murmur in the aortic area, an apex beat slightly displaced to the left, a normal blood pressure and a positive Wassermann reaction. A diagnosis of 'syphilitic aortitis with angina' was made. The electrocardiograms showed right bundle-branch block.

Cases of similar nature had also been observed at the Liverpool Heart Hospital, but the case reports of these are, unfortunately, not available. In some of the cases a coexistence of both types of anginal pain (*viz.*, Heberden's angina and aortalgia) was noted.

*Case 4.*—L. S., a Hindu male, married, aged 55, gave a three months' history of breathlessness on exertion, insomnia and cough with expectoration. The symptoms started soon after a febrile attack.

The pulse rate was 85 per minute, and the blood pressure 210/140. The urine contained albumin but no casts. There was some oedema of the ankles, the neck veins were congested and pulsating and the liver edge was palpable and tender.

For some time, he had experienced severe sub-sternal pains on exertion or walking, and lasting for fifteen to twenty minutes; they would start behind the upper half of the sternum and would radiate to the left shoulder alone or to both shoulders, but never below the level of the elbows. The attacks of pain were succeeded by tenderness and cutaneous hyperalgesia, lasting as long as twenty-four hours, over the entire length of the sternum, in the left inter-scapular region and over the brachial plexus in the left axilla. These regions would remain hyperæsthetic to painful stimuli for hours after each attack of pain.

The patient was considerably benefited by rest in bed and a sedative mixture for some weeks; when last seen in October 1939, he was free from pain and his blood pressure was 180/120.

### Discussion

*Diagnosis.*—At first sight, there appears to be little or no dissimilarity between cases of true angina pectoris and aortalgia. They both have sub-sternal pains with a tendency to radiate into the arms; closer scrutiny, however, reveals differences between the two types of pain, sufficiently characteristic to permit differential diagnosis:—

1. In aortalgia, radiation of pain frequently occurs into both arms; in angina, on the other hand, the pain is nearly always confined to one arm only, usually the left.

2. Radiation of pain below the level of the elbow is rare in aortalgia; in angina, it frequently radiates along the ulnar aspect of the forearm to the inner two digits of the hand.

3. The pain tends to be located higher in aortalgia, being usually behind the upper third of the sternum; true anginal pain is most frequent behind the middle third of the sternum.

4. Feelings of anxiety or *angor animi* are unusual in aortalgia; the patient may, however, experience a feeling of 'choking' in the neck.

5. Tenderness to pressure over the left brachial plexus is a feature characteristic of aortalgia, as shown by Schmidt; three of the cases reported here presented this feature.

6. In aortalgia, a band or zone of hyperæsthesia or hyperalgesia often appears in the inter-scapular region at the back, usually to the left of the mid-line and in the distribution of the second, third and fourth thoracic segments of the cord.

7. Pain, as a rule, tends to last longer in aortalgia than in angina.

8. Sequelæ, such as feelings of numbness or tingling, are more persistent and intractable in aortalgia.

9. Transitory electrocardiographic alterations (e.g., inversion of the T waves), described during attacks of angina, have not been observed in aortalgia.

*Causation.*—Aortalgia is secondary to diseased conditions of the aorta, usually of the nature of syphilitic aortitis or atherosclerosis. It has been suggested by some German workers that mere increase in the tension of the walls of the aorta may lead to the symptoms of aortalgia.

Libman (1926) has maintained, in spite of opinions to the contrary, that essential hypertension, even in the absence of coronary disease, can cause angina pectoris. It is conceivable that some, if not the majority, of anginal attacks encountered in uncomplicated essential hypertension are of the nature of aortalgia and induced by increased tension on the walls of the aorta, in that disease.

The tendency, at the present day, is to attribute angina pectoris, in accordance with Burns' (1809) theory, to myocardial anoxæmia resulting from coronary disease. Well-known authorities like Allbutt (1915) and Wenckebach (1924) have, on the other hand, supported the aortic theory of origin of angina. Considerable evidence has been put forward in order to substantiate each of these theories of angina; in the face of such evidence, it is highly probable that angina may, in fact, have a dual origin; though of coronary origin in most cases, it may, at times, be secondary to diseased conditions of the aorta. Such a possibility has been suggested by several authors on the subject. Whether the angina of aortic origin can be clinically distinguished from that of coronary origin and whether angina of aortic origin always conforms to the clinical description of aortalgia, presented above, are problems which remain unsolved. These matters are in need of further

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## STUDIES IN THE EPIDEMIOLOGY OF PLAGUE IN H. E. H. THE NIZAM'S DOMINIONS: COMPARISON OF CERTAIN FACTORS IN A PLAGUE-INFECTED PLACE WITH THAT OF NEIGHBOURING PLAGUE-FREE AREA

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THE geographical distribution of plague has never been uniform throughout the world at any time, even during different pandemics. Some places were affected badly, some suffered only from mild epidemic outbreaks, while still some others were fortunate enough to escape altogether from the ravages of this disease. India has been no exception to this phenomenon. Here almost the entire east coast and practically the whole of Eastern Bengal and the Province of Assam have been, so far, free from plague infection.

During the last pandemic, the freedom from plague enjoyed by most of the European countries is attributed to the improvements that have taken place in the last two centuries in environmental and personal hygienic conditions which make the association of the rodents with human beings more difficult. Still, one is at a loss to explain satisfactorily why certain places escaped plague infection during the previous pandemics, when the general sanitary conditions in those countries were not very different from those to be found at present in the countries where plague is still prevalent. The causes for the subsidence or the ultimate disappearance of the pandemics also are not very clear at present.

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investigation and are likely to modify considerably our present-day views on the genesis of anginal pain.

### Summary

1. Four cases of angina of an unusual type are presented; they conform to the clinical description of 'aortalgia' furnished by German authors.

2. The diagnostic criteria for the condition (aortalgia) are given and its causation briefly discussed.

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The Advisory Committee on Plague in India (1911) tried to explain the freedom of East Bengal and Assam to plague infection to the following causes :—

1. Peculiarities of geographical situation and difficulty of means of communication from place to place, particularly during monsoons.

2. Habits of the people and the nature of the construction of the houses and huts were such as to render suitable shelter and food for rats difficult.

3. Presence of a large number of *Crocidura coerulea* (musk rats) which are natural enemies of rats. However, in their later reports, the Commission left the question open by stating that the freedom from plague enjoyed by some places might be due to other factors unexplainable at present.

Hirst in 1912 described a newly-discovered species of xenopsylla, viz, *X. astia* and he subsequently found that the rats of two of the principal cities of the Orient, Colombo and Madras, were infested with *X. astia*, exclusively.

Philip and Hirst (1917) carried out their first series of experiments on the transmission of plague with *X. astia* with negative results and put forward the hypothesis that the relative freedom of Ceylon and certain parts of South India from plague was to be attributed to the relative inefficiency of *X. astia* as a vector of plague both from rat to rat and from rat to man.

Later experiments of Hirst (1926) showed that the climatic factors, particularly temperature and relative humidity, had varying effects on the developmental stages, as well as on the transmission mechanism of the different species of rat-fleas.

Goyle (1928), on the other hand, showed that in the United Provinces of India the predominance of *X. astia* and a fairly severe incidence of plague in a place were not incompatible. To him it appeared that proximity to infected places and facilities for communication with them were more important than the flea-species factor in determining the incidence of plague.

So far in this connection, that is the comparison of the plague-infected with plague-free places, only such places have been compared that are situated at a great distance from one another. It was thought that more useful information could be obtained if such plague-infected and plague-free places were to be compared that were situated quite close to and in free communication with one another.

Two such places in H. E. H. The Nizam's Dominions are Hyderabad city (plague-infected) and Nalgonda (plague-free).

Hyderabad city was first infected with plague in the year 1911. During the first 10 years there were four severe epidemics of plague with

intervals of plague-free years (*vide*, table I). Since then moderately severe or mild epidemics have been more or less the annual feature of the city. From Hyderabad city the infection spread to many places in the western half of the Nizam's Dominions\* while several places in the eastern half, known as the *Telangana* area, in spite of imported cases have remained so far free from infection, Nalgonda, a district headquarters town about 64 miles from Hyderabad, is a typical example of the places in the latter category.

TABLE I

*Plague incidence in the city of Hyderabad-Deccan*

Year	Attacks	Deaths
1911-1912 ..	18,478	16,901
1912-1913 ..	..	..
1913-1914 ..	..	..
1914-1915 ..	..	..
1915-1916 ..	16,983	14,980
1916-1917 ..	..	..
1917-1918 ..	..	..
1918-1919 ..	..	..
1919-1920 ..	2,414	1,834
1920-1921 ..	6,330	5,148
1921-1922 ..	943	694
1922-1923 ..	..	..
1923-1924 ..	248	181
1924-1925 ..	7,600	6,301
1925-1926 ..	3,437	2,554
1926-1927 ..	260	194
1927-1928 ..	6,254	5,015
1928-1929 ..	1,335	905
1929-1930 ..	599	410
1930-1931 ..	1,780	1,132
1931-1932 ..	..	..
1932-1933 ..	1,762	1,101
1933-1934 ..	318	188
1934-1935 ..	679	410
1935-1936 ..	328	193
1936-1937 ..	535	270
1937-1938 ..	92	48
1938-1939 ..	207	104
TOTAL ..	70,582	58,563

A thorough rat-flea survey of Hyderabad city was carried out and the results published some time back (Walker, Chenoy, and Rao, 1931). The results of this survey were as follows. Of the rodent population of the city 74.4 per cent. belonged to the species *Rattus rattus* and 24.9 per cent. to *Mus musculus* (mice). The rest (less than one per cent.) consisted of *Gunomys varius* (field rats), *Crocidura coerulea* (musk rats) and *Bandicoota indica*. Of the 13,743 fleas examined, 12,994 (94.2 per cent.)

\* Though some districts in the western part of the Dominions, bordering on the Bombay Presidency, were infected as early as 1898, yet it was not till Hyderabad city itself was infected that plague began to spread throughout this area, first cases being generally the imported ones from the city.

3. The pain tends to be located higher in aortalgia, being usually behind the upper third of the sternum; true anginal pain is most frequent behind the middle third of the sternum.

4. Feelings of anxiety or *angor animi* are unusual in aortalgia; the patient may, however, experience a feeling of 'choking' in the neck.

5. Tenderness to pressure over the left brachial plexus is a feature characteristic of aortalgia, as shown by Schmidt; three of the cases reported here presented this feature.

6. In aortalgia, a band or zone of hyperæsthesia or hyperalgesia often appears in the inter-scapular region at the back, usually to the left of the mid-line and in the distribution of the second, third and fourth thoracic segments of the cord.

7. Pain, as a rule, tends to last longer in aortalgia than in angina.

8. Sequelæ, such as feelings of numbness or tingling, are more persistent and intractable in aortalgia.

9. Transitory electrocardiographic alterations (e.g., inversion of the T waves), described during attacks of angina, have not been observed in aortalgia.

*Causation.*—Aortalgia is secondary to diseased conditions of the aorta, usually of the nature of syphilitic aortitis or atherosclerosis. It has been suggested by some German workers that mere increase in the tension of the walls of the aorta may lead to the symptoms of aortalgia.

Libman (1926) has maintained, in spite of opinions to the contrary, that essential hypertension, even in the absence of coronary disease, can cause angina pectoris. It is conceivable that some, if not the majority, of anginal attacks encountered in uncomplicated essential hypertension are of the nature of aortalgia and induced by increased tension on the walls of the aorta, in that disease.

The tendency, at the present day, is to attribute angina pectoris, in accordance with Burns' (1809) theory, to myocardial anoxæmia resulting from coronary disease. Well-known authorities like Allbutt (1915) and Wenckebach (1924) have, on the other hand, supported the aortic theory of origin of angina. Considerable evidence has been put forward in order to substantiate each of these theories of angina; in the face of such evidence, it is highly probable that angina may, in fact, have a dual origin; though of coronary origin in most cases, it may, at times, be secondary to diseased conditions of the aorta. Such a possibility has been suggested by several authors on the subject. Whether the angina of aortic origin can be clinically distinguished from that of coronary origin and whether angina of aortic origin always conforms to the clinical description of aortalgia, presented above, are problems which remain unsolved. These matters are in need of further

(Continued at foot of next column)

## STUDIES IN THE EPIDEMIOLOGY OF PLAGUE IN H. E. H. THE NIZAM'S DOMINIONS: COMPARISON OF CERTAIN FACTORS IN A PLAGUE-INFECTED PLACE WITH THAT OF NEIGHBOURING PLAGUE-FREE AREA

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THE geographical distribution of plague has never been uniform throughout the world at any time, even during different pandemics. Some places were affected badly, some suffered only from mild epidemic outbreaks, while still some others were fortunate enough to escape altogether from the ravages of this disease. India has been no exception to this phenomenon. Here almost the entire east coast and practically the whole of Eastern Bengal and the Province of Assam have been, so far, free from plague infection.

During the last pandemic, the freedom from plague enjoyed by most of the European countries is attributed to the improvements that have taken place in the last two centuries in environmental and personal hygienic conditions which make the association of the rodents with human beings more difficult. Still, one is at a loss to explain satisfactorily why certain places escaped plague infection during the previous pandemics, when the general sanitary conditions in those countries were not very different from those to be found at present in the countries where plague is still prevalent. The causes for the subsidence or the ultimate disappearance of the pandemics also are not very clear at present.

(Continued from previous column)

investigation and are likely to modify considerably our present-day views on the genesis of anginal pain.

### Summary

1. Four cases of angina of an unusual type are presented; they conform to the clinical description of 'aortalgia' furnished by German authors.

2. The diagnostic criteria for the condition (aortalgia) are given and its causation briefly discussed.

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\* Frank, L., and Worms, W. (1926). *Deut. Med. Woch.*, Vol. LII, p. 570.  
Libman (1926). *Trans. Assoc. Phys.*, Vol. XLI, p. 305.  
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chief railway station through which both the import and the export trade is carried on is Bhongir, on H. E. II. the Nizam's State Railway broad-gauge line. It is 48 miles from Nalgonda, with which it is connected by a metal road

*Housing conditions.*—The town proper between the two hills is thickly populated. Houses are built quite close together, the intervening lanes being very narrow and dirty. There are no drains except on the main roads. The houses of the middle and the well-to-do class of people have country-tile roofs, while the rest have only thatched roofs. The *gunjes* (grain godowns and markets) though built separately are heavily rat-infested. The extended town in the Rambiri Mohalla possesses fairly good sanitary conditions with better types of bungalows and houses.

*Plague history of Nalgonda.*—No indigenous case of plague has been reported as yet from Nalgonda. Occasionally, a few cases were imported from the neighbouring infected places, such as Hyderabad and Bhongir, but these never gave rise to any indigenous case or rat-mortality.

*Method of work.*—The whole town was divided into sections roughly corresponding to the municipal wards. Modified double-chamber 'Wonder' traps were laid for one day by turn in each of these sections, with the exception of the *gunj* area where they were laid for 3 days. In each section or ward the houses or shops were selected for trapping in such a manner as to give a thoroughly representative sample of that section. Two coolies aided by a sanitary sub-inspector distributed these traps in the selected houses every evening. These traps were cleaned with water thoroughly every third day and on the other days were only exposed to light and air for a few hours in the locality. This method of cleaning, traps in the experience of the plague department in Hyderabad has proved very efficient. Washing the traps every day did not prove any improvement, while smearing the traps with mustard oil or any other oils distinctly reduced their value as rat-traps. Besides, this would have also interfered with the flea survey work by some of the fleas adhering to the traps and thus escaping notice.

A uniform bait of dough made from wheat flour was used in all these traps throughout the survey. Traps were collected from the houses in the early morning and those traps that contained single rodents were immediately covered with a clean white canvas bag and sent back to the field laboratory, temporarily located in the compound of the local civil hospital, for the collection of fleas.

The traps, covered with bags, were transferred here to an air-tight wooden box in which they were exposed to petrol vapour. This not only killed the rats but also killed all the fleas on them in about half an hour's time. After this interval, the traps with the bags were slowly removed and placed over a table with raised

edges and covered with a white water-proof sheeting (*vide* fig. 1). The bag was then removed from the trap and all the fleas in the bag were collected. The rat was then taken out of the trap and combed. Any fleas that fell out during the process of combing were added to those that were collected from the bag. Finally, the rat was thoroughly beaten on the table to let loose any fleas still adhering to it. It was only rarely that this additional process of beating or hammering of the rats on the table yielded an additional flea or two. The fleas from each rat were collected in a separate test-tube labelled with the date and the species of the rats from which these fleas were collected. The following method of clearing these fleas for identification purposes was adopted. The fleas were first heated gently in a test-tube with rectified spirit for two or three minutes to de-hydrate them

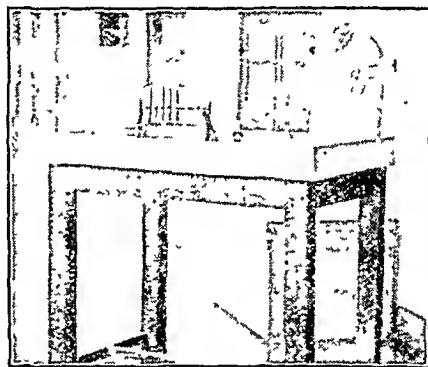


Fig. 1.—Nature of the table used for the collection of fleas.

completely and they were then cleared by again gently heating them in aniline oil for two minutes. They were mounted on a slide in balsam and examined under a low-power microscope. This process rendered the fleas fairly clear so as easily to show their typical characteristics for the purpose of identification.

All the dead rats from which the fleas had been removed were then dissected to find out any macroscopic signs of acute, chronic, or resolving plague. Smears were made from the spleen, liver and heart blood and stained with carbol thionin and by Gram's method and examined under the microscope for the presence of *Pasteurella pestis*.

*Rats.*—Details are given in table II. Total number of rodents trapped was 152, of these only two were mice and the rest *Rattus rattus*. Female rats were found in larger numbers than male rats. The density of rat population was not only high in the *gunj* and bazar area, but also in some of the residential quarters, such as Hajjamwadi and Dhedwadi. The high density of the rat population in these areas is due to the housing conditions of these localities. Houses, both on account of the nature of their construction, as well as the habits of the inmates, afford ample shelter and food for rats.

were *X. cheopis*, and the rest (792 or 5.8 per cent) were *X. astia*.

To compare the rat and flea factors of this plague-infected city with those of Nalgonda, a rat-flea survey of this latter place was undertaken by the author and the following is a short summary of the survey report :—

been 25 inches. During the period of survey the meteorological conditions were as follows :—

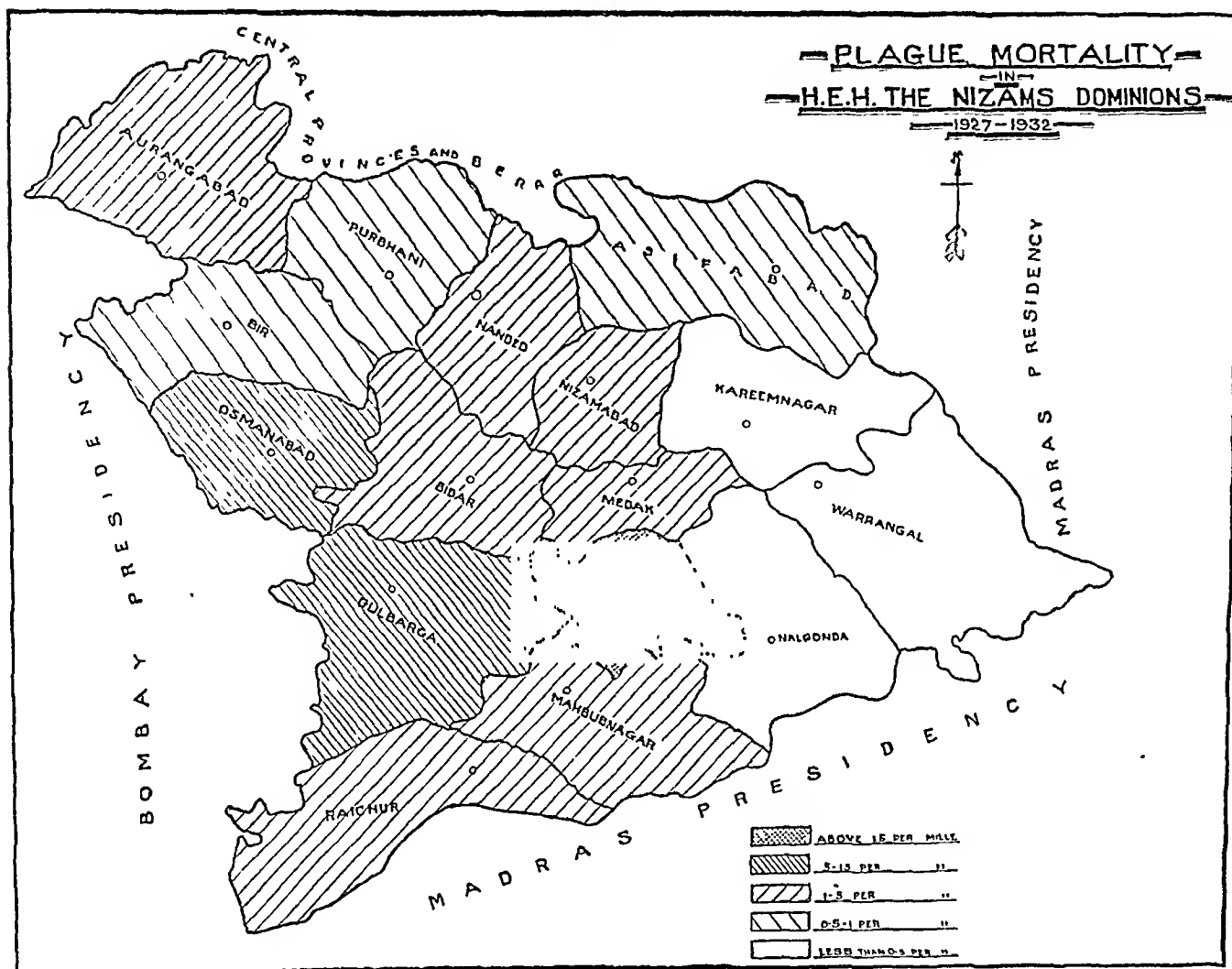
Mean dry-bulb temperature at 8 a.m. 94.2°F.

Mean wet-bulb temperature at 8 a.m. 76.0°F.

Mean relative humidity 39 per cent.

Mean saturation deficiency 0.984 in.

#### MAP



#### Rat-flea survey of Nalgonda

*Geographical situation.*—Nalgonda town is the headquarters of the district of the same name and has a population of 10,058. It is situated 79° 14' 57" N. and 17° 4' 9" E. The town proper is located between the two hills lying on its northern and southern sides.

There are two small tanks within the municipal limits, but they are dry during most of the year. Two miles from the town is the largest tank of the district, known as the Pangal tank. Quite close to the tank is Pangal village where several old temples with beautiful sculptures and stone inscriptions of archaeological interest are to be found.

Survey work was commenced on 12th May, 1931, and closed on the 19th of the same month.

The climate of this place is generally hot and dry. Average rainfall for the last five years has

Maxim temperature recorded during the period was 110.5°F. and the minimum 82.0°F.

Both wet and dry cultivations are carried out round about the town. The chief agricultural products of the neighbouring places are rice, *jawar*, *bajri*, and castor seeds.

*Exports and imports.*—The chief exports from this place in order of importance are castor seeds, rice, *bajri*, tobacco, cotton and onions. Oil seeds are exported chiefly to Bombay and occasionally to Cocanada. The imports are wheat and jaggery from the Punjab, salt from Bombay, chillies from Warrangal and also to a certain extent from the neighbouring villages, kerosine oil from Madras, and other substances, such as pulses, turmeric, sugar and *jawri* (white), either directly from places where they are produced or more often from wholesale merchants both at Hyderabad and Bhongir. The

TABLE IV

Results of experiments for testing the resistance of Hyderabad and Nalgonda rats to plague infection

Locality and the species of the rats tested	Duration of the experiment	Number of organisms inoculated into each rat	Total rats tested	NUMBER OF RATS THAT DIED ON DAYS SHOWN													Number of rats survived	Mortality per cent
				1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th		
1. Hyderabad— <i>Rattus rattus</i>	27th April to 18th May.	2,625	40	..	..	3	5	12	3	6	..	..	1	..	..	2	8	80.0
<i>Rattus rattus</i>	11th May to 1st June.	170	60	..	..	..	7	10	8	6	6	5	2	2	..	..	14	76.7
TOTAL ..			100	..	..	3	12	22	11	12	6	5	3	2	..	2	22	78.0 ± 4.1
2. Nalgonda— <i>Rattus rattus</i>	27th April to 18th May.	2,625	40	..	..	2	9	9	3	4	5	1	..	1	1	..	5	87.5
<i>Rattus rattus</i>	11th May to 1st June.	170	50	..	..	..	12	12	5	6	5	3	1	1	..	1	4	92.0
TOTAL ..			90	..	..	2	21	21	8	10	10	4	1	2	1	1	9	90.0 ± 9.0
3. Madras— <i>Rattus rattus</i>	27th April to 18th May.	2,625	10	..	..	..	..	4	3	2	..	..	..	..	..	..	1	90.0
<i>Rattus rattus</i>	11th May to 1st June.	170	10	..	..	..	1	3	..	2	..	1	..	2	..	..	..	100.0
TOTAL ..			20	..	..	..	1	7	3	4	..	1	..	2	..	..	1	95.0 ± 4.8
4. Bombay— <i>Rattus rattus</i>	11th May to 1st June.	170	10	..	..	..	1	..	..	..	..	..	..	..	..	..	9	10.0 ± 3.0

From the above results it appears that Nalgonda rats are as susceptible as Madras rats, while Hyderabad rats in spite of the long-continued severe infection have not attained the same amount of resistance to plague infection as that of Bombay rats. The difference between the mortality rates of Hyderabad *R. rattus* and Nalgonda *R. rattus*, though small (11 per cent), is significant, the standard error of this difference being  $\pm 4.49$ . The difference in the mortality rates between Nalgonda *R. rattus* and Madras rats ( $6.0 \pm 5.9$ ) suggests that this small difference may have occurred by chance, and that the samples are not probably different as far as their power of resistance to plague infection is concerned.

A remarkable fact in these experiments to be noticed was that the average duration of the illness was the same in all fatal cases, irrespective of the place from which the rats came (Bombay excepted, on account of small number of rats examined) and the average amount of the resistance to infection found in the group as

a whole. This shows that probably in all the places examined there are different strains of rats, some susceptible and some resistant, and that the susceptible strains from all places behave in the same manner, irrespective of the amount of the previous experience of plague that the place has had.

#### Discussion

Of the several factors concerned in the epidemiology of plague, the species of fleas present and the prevailing climatic conditions seem to play a very important rôle.

Though both *X. astia* and *X. cheopis* can transmit plague under favourable conditions, the former appears to be more sensitive to climatic variations than the latter. The Indian Plague Commission of 1908 showed that infected rat-fleas clear themselves of plague bacilli much more rapidly at 90°F. than at lower temperatures and also that a greater proportions of successful transmissions can be obtained at temperature below 85°F. The Plague Commission,

All the rats trapped were autopsied but none of them showed any signs of plague in any form (acute, chronic, or resolving).

these two places. They were quarantined for ten days in Hyderabad so as to exclude the chance of any naturally-infected plague rats

TABLE II  
Rat density in Nalgonda

Serial number	Locality	Number of traps set	Number of rats caught	Rat-density*	R. rattus		Mus. musculus (mice)	
					Male	Female	Male	Female
1	Latifgunj ..	150	84	56	29	54	..	1
2	Shah Bazar ..	50	21	42	8	13	..	..
3	Dhedwadi ..	25	13	52	4	9	..	..
4	Hajjamwadi ..	25	15	60	6	9	..	..
5	Telangana Mohalla ..	25	8	32	3	5	..	..
6	Dhangar Mohalla ..	20	6	30	2	4	..	..
7	Ramgiri Mohalla ..	5	..	..	..	..	..	..
8	Bhimpet ..	50	5	10	2	2	..	1
TOTAL ..		350	152	43.4	54	96	..	2

\* Rat-density in this table means the number of rats caught for every 100 traps set.

*Fleas.*—Details are given in table III. Total fleas caught on rats were 332. The two mice caught did not have any fleas on them. All those fleas belonged to the species *X. astia*. One hundred and thirty-seven were male fleas and the rest females. The flea index was high in

being included among them. They were then taken to the Haffkine Institute, Bombay, by train in two different cages.

After allowing another week's rest in Bombay for these rats to overcome the effects of the journey, altogether 100 rats from Hyderabad

TABLE III  
General and the specific *Rattus rattus* flea-indices in Nalgonda

Serial number	Locality	Rattus rattus examined	Fleas found	X. astia		Astia index	X. cheopis		Cheopis index
				Male	Female		Male	Female	
1	Latifganj ..	83	181	83	98	2.1	..	..	..
2	Shah Bazar ..	21	100	37	63	4.7	..	..	..
3	Other localities	46	51	17	34	1.1	..	..	..
TOTAL ..		150	332	137	195	2.2	..	..	..

the Shah Bazar area and in the *gunjes*. In the residential quarters this index was comparatively low.

#### Susceptibility of rats to plague infection

As *Rattus rattus* formed the chief rat population of both Hyderabad and Nalgonda, it was decided to test these rats for their susceptibility or resistance to plague infection. This would also throw some light, it was thought, on whether severe continued infection for the last 29 years in Hyderabad has made any significant difference in the resistance of the rats of this place to plague infection as compared to that of the *R. rattus* from Nalgonda which has remained so far free from plague infection.

Accordingly rats were collected from different localities of Hyderabad and Nalgonda so as to form a really representative sample of rats from

and 90 rats from Nalgonda were inoculated with a test dose of plague bacilli. With each batch of these rats 10 *R. rattus* from Madras and with the second batch 10 *R. rattus* from Bombay were also included as controls. The standard test dose used was the same as is used in the Haffkine Institute at present and described by Sokhey and Maurice (1935) and Sokhey (1936). The results of these tests were as follows (see also table IV) :—

Place to which the rats belonged	Total number of rats tested	Rats died of plague	Mortality rate per cent
Hyderabad ..	100	78	78 ± 4.1
Nalgonda ..	90	81	89 ± 4.4
Madras ..	20	19	95 ± 4.8
Bombay ..	10	1	10 ± 3.0



Fig. 2a.

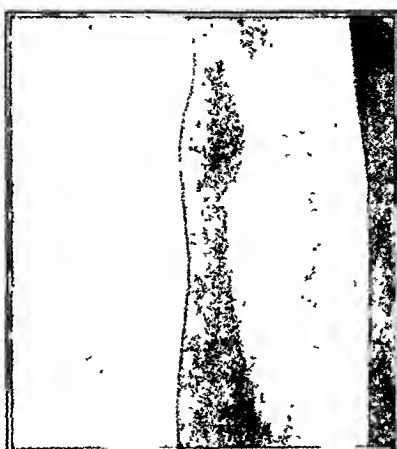


Fig. 2b.



Fig. 2c.



Fig. 1a.

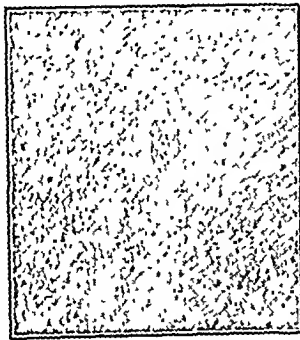


Fig. 1b



Fig. 4a.



Fig. 4b.



Fig. 3a

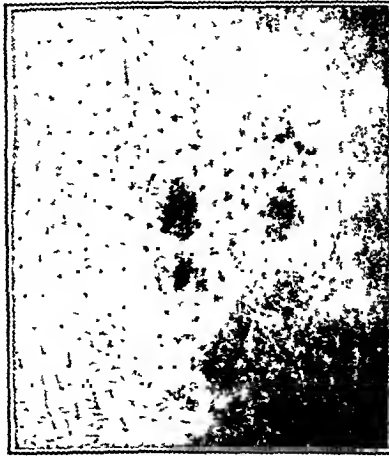


Fig. 3b.

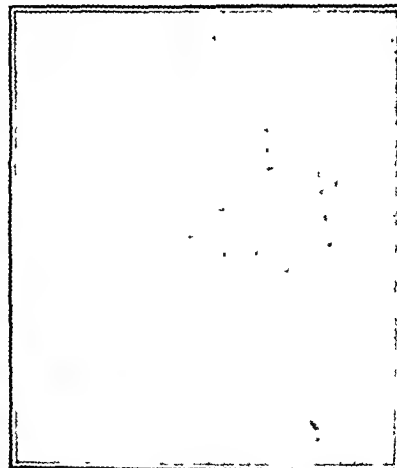


Fig. 3c.



though he had received a great fright, at the same time uttering an obscene epithet: I have observed that the obscene epithets are usually related to incest. They do not proceed to action and do not strike out as in type I. Even if they know that a person is standing behind or beside them they still react in the same manner. They are extremely ticklish.

#### *Allied complaints*

These include *latah*, *amok*, *banga*, *schamanismus* and *nat-win-de*.

*Latah*.—The description of the Malayan condition is taken from Palthi (*loc. cit.*).

'By *latah* is understood in Malayan countries a peculiar reaction to fright, which usually occurs among aged and uneducated women, and of which the most striking symptoms are a clouding of consciousness, echolalia and echopraxia.

A woman is called *latah* when by giving her a fright it is possible to throw her into such a condition that she repeats all words spoken to her, and imitates all actions performed before her with the purpose that she shall imitate them.

The patient remains in this condition as long as the examiner busies himself with her. Her state closely resembles a hypnotic *rapport* and frequently begins with the ejaculation of some obscene or meaningless word. If she is left alone or spoken to in a soothing way the peculiar condition of vacancy again subsides and she behaves like a perfectly normal person'.

The superintendent of the Singapore mental hospital has kindly supplied me with this and with several other references. He states 'I have not seen a case in the Singapore mental hospital, but the admissions are predominantly Chinese (68 per cent) (Tamil—16 per cent, Malay—10 per cent) and rural Malays are seldom seen. On the other hand the disease is certainly not prevalent, and is, I believe, becoming rarer as the older generation passes'.

*Amok*.—This is described as a psychical disturbance which develops into a violent attempt to kill people, succeeded by a stuporous condition no memory of which may be left; it occurs chiefly amongst Malays. The ætiology is stated to be a strong emotion of anger, sorrow or fear. The condition may be allied to epilepsy or epileptic equivalents.

*Banga*.—A hysterical condition which occurs chiefly amongst women about the age of puberty in the Belgian Congo. No stigmata of hysteria are displayed. It is accompanied by convulsions, uttering of wild cries and impulsive rushes into open country or jungle.

*Schamanismus*.—Certain Dayaks and other peoples throw themselves into a condition of excitement for religious purposes. Eroticism is displayed and they sing, shriek and dance to utter weariness. Resembles the dancing mania of the middle ages and therefore would appear to be related to *latah* according to Castellani and Chalmers (1910).

*Nat-Win-De*.—A yearly festival is held near Mandalay, is particular, and also in other parts of Burma, which is devoted to the worship of *Nats* (spirits) and of which the chief feature consists in a dance, usually by women and occasionally by men and young boys. The dance is started by a professional and it is quite unlike the usual Burmese dance. It is accompanied by swaying movements, with the eyes closed, which continues so long as they think they are possessed by *nat*. They have no recollection afterwards of what they have done. The dance is taken up by other people.

It is stated that old-time warriors have become spirits and take a liking for certain women. These women are then supposed to have fortune-telling powers. People pay them for their fortunes to be told.

Amongst other related conditions are the 'jumpers', the 'barkers', and the 'jerks', at various times described in Europe and also *Maladie de Gillis de la Tourette* of which the main symptoms are echolalia and coprolalia. The jumping Frenchman of Maine was described by Dr. Beard in 1880.

*Description of cases*.—Of the four cases described below, three belong to type I and one to type II.

*Case 1*.—A Burmese woman, aged 33, has been a patient in this hospital since 1928. She was admitted as an insane criminal having been acquitted of murder on the grounds of insanity. She murdered her husband with a *dah* (native knife) in the night without motive.

She was said to have had recurrent attacks of insanity for a period of four years before admission, and during these attacks she is said to have killed an ox with a *dah*, set fire to a hut, chased men, and been amorous towards them.

It is also stated that she had periods of somnolence during which she could not be roused, but that between these attacks she had been normal in her behaviour and rational in speech and had been able to procure for herself two husbands in quick succession. The first husband is said to have deserted her owing to her strange behaviour in these attacks.

She claimed complete amnesia for all these serious events in her attacks. At times she used to rush into the jungle, screaming and shouting for no reason; at others she beat her child causelessly and was aggressive. There is an interesting statement of a Burmese doctor to the effect that he used to treat her for her attacks of somnolence or trance-like sleeps.

On admission, she is stated to have had no symptoms suggestive of schizophrenia of that duration and no history of epilepsy. The doctor in his notes on admission said that the obscuration of consciousness, the trance-like states, amorous excitement and aggressiveness suggested the combination of a psychosis with a psychoneurosis.

I suggest that it is possible that we have here a condition similar to the *amok*.

There is no mention of any imitative signs, as in case 2, described in the notes taken on admission, but for some years it has been recognized that she imitates all actions performed in her presence and is very suggestible. It would appear that she suffered from this condition (*young-dah-hte*) before her admission as she says that it developed suddenly after seeing the blood of her murdered husband.

If she sees a person dance, she dances; if she is struck, she strikes the person by her side; if she sees one person kissing another, she kisses the person by her side; if tickled or startled she shouts and uses abusive languages. Another peculiarity about her is

*Present history.*—Two years ago, the patient suffered from fever with rigor for a fortnight and subsequently he noticed a hard swelling in the abdomen on the right side. Fever subsided and the swelling was much reduced. For the last six months he again had irregular fever and the swelling has again increased.

On examination a hard mass was palpable in the right hypochondriac region reaching below the level of the umbilicus. The upper surface was smooth, was felt below the costal margin, and definitely moved with the respiration. It was thought to be a case of enlarged liver and he was admitted into the hospital.

On subsequent examination after admission the following conditions were found—

(a) The swelling on the right side was typical of a spleen with a notch on the inner surface.

(b) Liver was found on the left side—normal in size.

(c) Heart sounds were missing on the left side, but on further examination it was found that they were present on the right side with the apex in the 5th right intercostal space three and half inches from the middle line. The cardiac dullness was also normal in size.

The patient was treated as an ordinary malaria case. The swelling became reduced in size and he left the hospital.

## EPIDERMOPHYTOSIS IN A VERY YOUNG CHILD

By L. M. GHOSH, M.B., D.T.M.

and

P. A. MAPLESTONE, D.S.O., D.Sc., M.B., B.S., D.T.M.

(From the Medical Mycology Inquiry, School of Tropical Medicine, Calcutta. Under the Indian Research Fund Association)

A HINDU girl, aged seven months, was brought to the out-patients department of the Calcutta School of Tropical Medicine, recently, for treatment of a skin condition.

The child had two ring-shaped patches on the back of the right shoulder. One patch was almost exactly



circular and about one and a half inches in diameter and the other slightly larger and irregular in outline extending to the posterior fold of the axilla (see figure).

Both patches exhibited raised margins composed of minute vesicles and they encircled areas of skin covered with fine scales; in other words they exhibited the typical appearance of lesions caused by an epidermophyton. Cultures from the scales confirmed the diagnosis because *Epidermophyton floccosum* (*E. cruris*) was isolated. Careful examination of the child's head failed to reveal any sign of trichophyton infection, and it was learned that the brother, who habitually carried his sister in his arms, had a ringworm infection of the body, which was the probable source of the child's disease.

*Discussion.*—None of the many standard works on dermatology available to us give any information on the age incidence of *E. floccosum* infection, but it is generally understood that young children are not affected by this fungus. As an instance of what may be taken as the opinion of dermatologists in general, Macleod (1933) says that *Tinea circinata* is essentially a disease of children and that the causative organism is a trichophyton spreading from the scalp. Further, our experience in Calcutta extending over more than fifteen years, during which period the annual average of new cases of ringworm of the glabrous skin was over 1,500, has been that no case has ever been seen before under ten years of age and the majority of them are adults. These facts emphasize the interest of the above record.

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## A HYDATID CYST IN THE NECK

By HUKAM CHANDRA, M.B., B.S., P.C.M.S.

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THE patient, an Indian Muslim male child aged 6 years, son of a weaver, was admitted into hospital on 9th October, 1939.

*History.*—Painless enlargement on left side of the neck; duration six months, causing no symptoms except slight inconvenience during mastication, yawning, etc., for the last six weeks or so. Past and family history nothing particular.

*Examination.*—An oval well-defined swelling with the long axis vertical extending from just below the ear to the supraclavicular fossa on the left side of the neck and measuring  $3\frac{1}{2}$  inches by  $1\frac{1}{2}$  inches. Outline smooth and regular, except at the lower pole where two almond-shaped cystic swellings distinct from each other and from the main tumour could be felt. The tumour was immobile but free from any adhesions to the overlying skin and was not tender to manipulation. Fluctuation was easily elicited but no fremitus or thrill was felt. Transillumination did not help. No enlargement of lymphatic glands in the neck, axillæ or groins was present. Physical examination of the rest of the body revealed nothing special. Liver and spleen were normal in size: no evidence of anæmia but differential count showed 6 per cent eosinophil cells; temperature was within normal limits; tongue clean and moist; oral hygiene satisfactory and appetite good; urine clear and stools normal; the general health of the boy was above the average.

Operation was performed on 11th October, 1939, under chloroform anaesthesia. The tumour was found beneath the sternomastoid muscle, the upper pole being under





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# THE CALL OF PAIN

The call of pain is seldom stilled, and relief is of primary importance to the suffering patient. The paroxysmal pain of dysmenorrhœa, the persistent and intense throbbing of migraine, the shooting pains of neuralgia, the pain in affections of the bones and joints, the pain resulting from accidents—all these, and many other conditions, yield with impressive readiness to the sedative and analgesic efficacy of Veganin. With Veganin there is no systemic disturbance, no habituation. It may therefore be safely entrusted to the patient as a dependable means of relieving and preventing pain.

# VEGANIN TABLETS

*Prepared by WILLIAM R. WARNER & CO. LTD., LONDON, ENGLAND.*

the parotid gland. The ectocyst was thin and firmly adherent to the carotid sheath. The cyst was enucleated easily with practically no bleeding. The fluid was slightly opalescent, specific gravity 1.008 with a trace of albumin, and characteristic hooklets were observed microscopically. The two cysts at the lower pole were separate from the bigger one with no general cyst wall.

The wound healed by first intention and the patient was discharged on the 27th October, 1939.

The point of interest is the rarity of the condition in such a site.

I am grateful to Major S. Smythe, I.M.S., Civil Surgeon, Multan, for his permission to publish the report of this case.

### ACUTE OBSTRUCTION CAUSED BY MECKEL'S DIVERTICULUM

By NAZIR AHMED BHUTTA, M.B., B.S., P.M.S.

*Assistant Surgeon, In-charge Civil Hospital,  
Dera Ismail Khan, N.-W. F. P.*

*History.*—A foot constable, aged 29 years, attached to a police station about 20 miles from headquarters reported sick to the dispensary doctor on the morning of 14th October, 1939. He gave him an enema and fomentations on the abdomen as he complained of pain in the abdomen and constipation with no passage of flatus for the last 24 hours. The man passed some faecal matter but no flatus and pain was not relieved. He was kept in the local hospital for more than 36 hours and then at 4 a.m. on 15th October was transferred to the police hospital from where he was sent to the civil hospital as an emergency case, at 9 a.m. the same day. He complained of severe irregular pain in the lower half of the abdomen, no passage of flatus or stools (except the small one in hospital) for three days, and vomiting.

He lay curled up in the bed, with thighs flexed and he had rapid thoracic type of breathing, pinched facies, coated, furred, dry tongue, temperature 99°F., and pulse 100 per minute. He vomited once on arrival but it was not faecal in character. Abdomen was tympanitic and no tumour was felt. There was no tenderness over McBurney's point, but there was deep-seated pain on pressure in the mid-line below the umbilicus. A gurgling noise was only occasionally heard with the stethoscope. There was no ladder-like appearance of the abdomen so typical in acute obstruction. Hernial sites were normal. Rectal examination revealed nothing of importance. A provisional diagnosis of 'acute abdomen' with obstruction and possible early peritonitis was made.

Atropine sulphas gr. 1/75 was given hypodermically and patient prepared for immediate operation, as palliative measures had previously been tried in the police hospital and rural dispensary and failed. Under general anaesthesia by chloroform the abdomen was opened by a para-rectal incision and explored. Purulent free fluid was present and the intestines were covered with exudate; the lower coils of the ileum were found tightly strangled by what appeared to be an unusually long appendix, but further search showed the appendix to be quite distinct and perfectly healthy.

The strangulating band (as it appeared at first) was encircling two coils of the intestine which were doubled up. On one side, which was thin, it was attached to a cord-like peritoneal band connecting it with the abdominal wall; this was the cause of obstruction. On cutting this band it was found to be a Meckel's diverticulum very much stretched and gangrenous. After untying the knot in the diverticulum, in which considerable trouble was experienced to avoid bursting it, the obstructed coils returned to normal colour after a few minutes' fomentation with saline. The proximal end of the diverticular attachment to the intestine was crushed with long artery forceps, cut and invaginated inside the gut by purse-string sutures, after application of carbolic acid.

Then after the usual peritoneal toilet the abdomen was closed in layers and a drainage tube was put in reaching down to the pelvic cavity.

The patient afterwards was put on fluids by mouth and rectum, and placed in Fowler's position.

Not more than 20 c.cm. of anti-gas-gangrene serum and antiperitonitis serum was available. He was very restless in the afternoon and hyoscine hypodermically had to be administered at night and bromide was put in the rectal saline, but he was still uncomfortable that night and the abdomen became distended. On the following day pitressin (P. D. and Co.) 1 c.cm. hypodermically every four hours was started and an enema of glycerine was given. This day he was again uncomfortable but at night he passed some flatus. On the 17th morning he passed a good motion and a large amount of flatus and henceforward he progressed and made an uneventful recovery except for a stitch abscess.

### M. AND B. 693 IN A CASE OF PNEUMONIA COMPLICATING A CASE OF STAB WOUND OF ABDOMEN

By NAZIR AHMED BHUTTA, M.B., B.S., P.M.S.

*Assistant Surgeon, In-charge Civil Hospital,  
Dera Ismail Khan, N.-W. F. P.*

*History.*—Male, aged 20 years, agriculturist was stabbed at about 8 a.m. on 25th November, 1939, by a person who ran amuck. He was picked up by the police and sent to the hospital.

On examination it was found that he was stabbed in the left anterior axillary line below the costal margin with omentum and small intestine protruding about 9 inches. Pulse 78, respiration 26, temperature 98°F. There were three punctures in the intestine. No injury to the chest was found. After adopting anti-shock measures, a laparotomy with paramedian incision and excision of protruding omentum, suturing of punctures and exploration of abdomen was done. The routine post-operative treatment for laparotomy was adopted and the following morning it was noticed that the patient was spitting blood-stained rusty sputum and had hurried respiration (42 per minute). His temperature was 100°F. and pulse 128 and he passed a motion and flatus. The lungs were examined and a few râles were found in the left chest. Antiphlogistine was applied and the pneumonia mixture of the hospital given. In the evening his condition rapidly became worse, temperature 102°F., pulse 136, respiration 56 and general condition very bad. Examination showed definite consolidation of the left base. The cause of pneumonia was either exposure in the village after the injury in a condition of panic, the anaesthetic or because the injury was near the left diaphragm. Immediately he was put on M. and B. 693 by the method advised in the wrapper, antiphlogistine was applied and expectorants and glucose water given.

I never expected him to live to the next day. His condition next morning was remarkably changed, respiration much easier, pulse also fuller and steadier. It came down to normal within 36 hours of commencing M. and B. 693. But the lung condition showed not much change and respiration remained up to 32 per minute for six days. He made an uneventful recovery.

In the Lady Reading Provincial Hospital, Peshawar, stab wounds of the abdomen are so common that in 1937 about 90 laparotomies were done because of them, and this complication (pneumonia) was presumably in many cases the cause of fatality rather than the original stab. It might possibly make some difference in the results of such cases if M. and B. 693 is used.

My thanks are due to Lieut.-Col. A. K. Sahibzada, I.M.S., civil surgeon, for permission to publish this report.

# Indian Medical Gazette

FEBRUARY

## THE TRANSMISSION OF KALA-AZAR

KALA-AZAR is a disease that has existed in India for at least a hundred years. Its earlier history is obscured by the fact that, in the days before the parasitic origin of disease was established, it was not unnaturally confused with other diseases in which fever and splenic enlargement were prominent symptoms, for example, malaria. However, the shrewd clinicians of seventy years ago, even before Laveran had demonstrated the malaria parasite, recognized kala-azar as a separate clinical entity, though it was not until the beginning of the present century that the causative organism was discovered. The next problem for the sanitarian—as distinct from the physician, for the latter was at that time faced with the heart-breaking problem of attempting to cure a disease that was almost invariably fatal whatever line of treatment was adopted—was to discover how the disease was acquired. A great deal of scientific attention was focussed on this problem, as kala-azar had for many years the distinction of being the only important tropical disease whose mode of transmission was not known. Such problems are not solved in the laboratory, as is popularly imagined, but in the field, for it is only by observing the conditions under which a disease is acquired, and the habits and mode of living of the people who suffer from it, that the first clues to the solution are found; kala-azar proved to be no exception.

It was apparent from the earliest days of observation that kala-azar was 'infectious'; it was a 'family' and a 'house' disease, and in the areas where it was epidemic the first cases in a village could often be traced to the arrival of a person suffering from kala-azar. Yet, whilst kala-azar seemed to spread from village to village in some areas, where certain physiographical and climatic conditions prevailed, it did not behave like many infectious diseases and spread from province to province and country to country; it did not, for example, spread to high altitudes, nor did it desert the alluvial plains of the Ganges valley and climb to the adjacent laterite plateau, though the people are of the same race and caste and the living conditions in the two areas closely resemble one another, and though there is repeated interchange of population. These distinctive traits of the disease made it difficult to believe that transmission from man to man was a direct one such as occurs in the case of bowel infections, like cholera, dysentery or typhoid, from excretory

contamination of food or water, and in respiratory diseases, such as the common cold or influenza, by droplet distribution from the respiratory tract; they suggested rather that the transmission of this disease is a more complicated biological process that can only occur in especially favourable circumstances. Insect transmission is such a process, and, as this is a method by which many diseases are known to be transmitted, it is very natural that the possibility that kala-azar also is transmitted in this way should have been envisaged.

Kala-azar is essentially a disease of rural areas, and, though it does occur in towns, the incidence is never as high; this is significant in view of the fact that large numbers of people densely packed together would form very suitable material for a conflagration, were the infection and the means of transmission from one person to another both present. It was observed that although there were in Calcutta innumerable people suffering from kala-azar who, in order to obtain treatment, had come in from the country districts round Calcutta, where the disease is very prevalent, the disease did not appear to spread except in one particular quarter, and this was not the most congested quarter of the town. This observation appeared to provide an excellent opportunity for studying conditions favourable to the transmission of kala-azar, with a control area nearby in which they were not favourable. There were obvious advantages in undertaking investigations in a circumscribed area where special conditions prevailed and where the flora and fauna, though numerous and varied, did not present to the investigator, who wished for example to take a census of the blood-sucking insects, the almost hopeless task that he would have had to face in the rural endemic areas. The constant presence of the parasite of kala-azar in the blood of the patient seemed to suggest the possibility that the parasite left the body by way of the peripheral blood, and in this connection the ubiquitous bed-bug had come under suspicion, but *vis-à-vis* the unusual epidemiology of the disease, its very ubiquity excluded it.

The sand-fly (*phlebotomus*) had already been incriminated in connection with the transmission of oriental sore—another leishmanial infection—and this genus was amongst the first to receive special attention; three species of *phlebotomus* were found in Calcutta, *Phlebotomus minutus*, *P. papatasi*, and *P. argentipes*. The first species is a common one but is almost entirely a non-mammalian-blood feeder; the second is rare and found only at certain seasons of the year; but the third one was not only found in large numbers but was far commoner in the endemic than in the control area.

The next stages in the investigation were undertaken in the hospital and laboratory. Although at this stage no infected sand-flies were found in nature (later, infected wild sand-flies were found on many occasions),



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## Special Articles

### HÆMATOLOGICAL TECHNIQUE

#### PART I

By L. EVERARD NAPIER, M.R.C.P. (Lond.)

and

C. R. DAS GUPTA, M.B. (Cal.), D.T.M.  
Calcutta School of Tropical Medicine

ANÆMIA is attracting more and more attention each year in India. Also it is being realized that accurate methods of blood examination are essential for the proper study of a case of anemia. Many books on laboratory technique give full details of the methods that can be adopted, but such books are not always easily available to practitioners: further, the methods described in these books are often embarrassing in their multiplicity. We feel that readers of this journal, particularly those working in India, might find a short description of the methods followed at the Calcutta School of Tropical Medicine useful, and we have therefore prepared a series of short notes on hæmatological technique, which we propose to publish in successive numbers of this journal.

#### (1) *The Collection of the blood sample*

The first essential is that one constant practice should be decided upon and followed. There is a difference between capillary, which for all practical purposes is arterial, and venous blood, but the difference is only of practical importance if two samples from the same individual at different times are to be compared, or when normal standards are being worked out.

As there are very distinct advantages in the use of venous rather than capillary blood, the former is preferred.

The advantages are that all the examinations, e.g., the estimation of hæmoglobin, the determination of cell volume, the total red and white cell counts, the reticulocyte count, the differential white cell count, the measuring of the red cell diameters, the icterus index, the van den Bergh reaction, the fragility test, the erythrocyte sedimentation test, etc., can all be done from a single sample of blood obtained by a single puncture. Further, the tests can be repeated by the same or by different workers from the same sample of blood.

For some of the tests, the van den Bergh test, for example, blood will have to be taken from the vein, so that sufficient might as well be taken at one time for all the tests and the patient saved a number of additional pricks. In weak and anæmic individuals, it is sometimes difficult

to draw enough blood from a finger or ear lobe without squeezing the part, and thereby diluting the blood with the tissue fluid.

The following rules should be observed when using venous blood:—

(a) The syringe should be air-tight and perfectly dry. The syringe is conveniently dried by first washing it thoroughly in clean water, removing the water with alcohol, removing the alcohol with ether, and finally drawing air through it. If there be even a trace of water or alcohol, there will be hæmolysis of the blood, and this will make it unsuitable for examination.

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*Time for collection of blood.*—When repeated examination is required, blood should always be collected at the same hour under basal conditions in the morning. Even for a single examination it is preferable to collect the blood in the morning under basal conditions; this precaution will minimize the effect of the fluctuations in the total and differential count due to muscular activity.

*Procedure.*—The blood is drawn from one of the prominent superficial veins at the bend of the elbow in a perfectly dry air-tight syringe.

First of all, smears for the differential leucocyte count and red-cell diameter measurements should be made\*; then a measured amount of blood is transferred to a small 25 c.cm. Erlenmeyer flask containing the requisite amount of anti-coagulant for that quantity of blood.

*Anti-coagulant.*—Two milligrammes of dry oxalate powder is required for each cubic centimetre of blood. A mixture of potassium and ammonium oxalate powder in the proportion of 2 to 3 has been found to be ideal, as, in the above proportion, the shrinkage caused by potassium oxalate is counteracted

\* As stated above this can be done from the oxalated sample, but it is better to make separate smears.

it was shown by serological testing of the blood meal of sand-flies that, in the absence of cattle, *P. argentipes* was a persistent human-blood feeder and that most of the flies of this species caught in the endemic area contained human blood. It was also found that laboratory-bred *P. papatasi* fed readily on man but *P. minutus* would not; the first experiments were therefore conducted with the two former species, and it was found that in a large percentage—over 40 per cent in the first experiments—of *P. argentipes* fed on kala-azar patients the parasite developed into the herpetomonas stage and caused a heavy flagellate infection in this sand-fly, whereas in *P. papatasi* only two per cent developed a light infection.

It was further shown that, when these flies were kept alive for about seven days after the infecting feed, they developed a heavy infection which tended to move forward to the anterior parts of the fly and eventually to form a large plug of flagellates in the buccal cavity. The successful march of these investigations was now checked, for experiments to transmit kala-azar by feeding infected flies on susceptible animals and on human volunteers all failed; later, however, in experiments conducted by two different groups of workers the infection was transmitted to several hamsters, but only after a very large number of negative experiments. All attempts to transmit the disease to human volunteers were unsuccessful, but this was not very surprising in view of the fact that man enjoys a natural resistance to the infection, which infection probably only establishes itself under special circumstances.

In the meanwhile, in other countries where kala-azar is endemic, China and Italy, for example, these observations of the workers in India were confirmed and it was shown wherever investigations were carried out that sand-flies of allied species capable of carrying the infection were to be found. In China, a slight diversion was caused by the observation that viable parasites could often be recovered from the nasal mucosa of kala-azar patients and the suggestion that the infection might be transmitted directly from person to person was again revived; however, the known epidemiological facts were so directly opposed to this theory that it could not be entertained seriously. Other observations were made, none of which proved, but all of which added support to, the sand-fly theory of transmission: the case for the sand-fly, *P. argentipes* and allied species, is well summarized in the following quotation from a recent publication:—'So far as India is concerned, every epidemiological observation fits in with the sand-fly hypothesis of transmission. Further, this sand-fly has actually been found in large numbers in every locality where kala-azar occurs; it is a persistent human-blood feeder; a large percentage of the flies that feed on an infected person acquire the infection; infected

flies have been found repeatedly in nature—this is not true of other sand-flies which are more prevalent in the non-endemic areas, nor of insects of any other genus so far experimented with; in this fly anterior development of the flagellate infection occurs and is unlikely to be purposeless—in natural flagellate infections which pass from insect to insect the development is usually posterior; and it has been shown experimentally that the fly is capable of transmitting the infection to a mammalian host by its bite. All these facts make it almost certain that this insect is an important agent in the transmission of the disease from man to man in nature, although it may not be the only agent'.

This then was the position about five years ago, and, as we appeared to be in an inter-epidemic period, research work on the transmission problem in India was virtually closed down, but, as during recent years there has been some evidence of a general increase in kala-azar in India, the nucleus enquiry was strengthened last year and work again commenced in a new locality where kala-azar was said to be increasing.

Elsewhere in this number will be found a paper reporting a distinct advance in the transmission problem. Hitherto in these experiments, sand-flies have been kept alive after their infective feeds on kala-azar patients by successive feeds on experimental animals, but now a technique has been devised for keeping the sand-flies alive by feeding them on fruit juice. It has been found that flies fed by this means live longer, and, further, that the flagellate infection in these flies develops more rapidly until the anterior part of the alimentary tract becomes so completely blocked that the fly is incapable of taking a blood meal, even though it buries its proboscis into the skin and makes violent attempts to withdraw blood. It seems inevitable that this violent muscular effort on the part of a 'blocked' fly to take a blood meal must lead to the dislodgement of some part of the plug of flagellates, which would then find its way into the wound.

Heavy infection of a sand-fly was reported in the earlier investigations, and this mechanism of transmission was suggested, but the recent investigations have shown how these heavy infections can be produced with considerable regularity in circumstances which will frequently be reproduced in nature. Finally, the few transmission experiments with hamsters that have been carried out since this observation was made have shown a much higher proportion of successes than has been achieved hitherto.

Whilst it cannot be claimed that these new observations have proved the sand-fly theory of transmission, or even that they have carried the investigations through another stage, they have explained certain apparent anomalies and have added considerable support to a theory which has already been accorded general acceptance.

## Special Articles

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by ammonium oxalate (Wintrobe and Landsberg, 1935). To measure the requisite amount of the oxalate powders make a 1 per cent solution of the two oxalate powders, ammonium and potassium; accurately measure with a pipette 0.4 c.cm. of the potassium salt and 0.6 c.cm. of the ammonium salt, and put them into the flask; evaporate in a dry oven, after which the oxalate will be found at the bottom of the flask in a powdered state; this is the amount required for 5 c.cm. of blood; for 3 c.cm. the proportions will be 0.24 c.cm. potassium and 0.36 c.cm. ammonium salt. The flasks are now kept corked and are ready for use.

It is a good practice to have two sets of flasks prepared containing enough anti-coagulant for 5 c.cm. and 3 c.cm., respectively.

If potassium oxalate alone is used, 2 milligrammes are required for each cubic centimetre of blood, that is, 10 milligrammes or 1 c.cm. of one per cent solution for each 5 c.cm. of blood. If potassium oxalate only is used, Wintrobe's correcting factor  $\times 1.09$  must be applied to compensate for shrinkage.

*Time limits.*—Osgood and others (1931) give the following time limits for different examinations:—

Hæmoglobin estimation, red cell count, white cell count, and reticulocyte count—24 hours.

Icterus index and van den Bergh test—2 hours.

Cell volume, fragility test, and sedimentation rate—3 hours.

Making smears for differential count—1 hour.

## (2) Estimation of hæmoglobin

To estimate the amount of hæmoglobin in any sample of blood advantage is taken of certain properties of hæmoglobin. Of these the most important is its oxygen-carrying capacity. A fixed amount of hæmoglobin will always combine with the same amount of oxygen, actually 1 gramme of hæmoglobin with 1.34 c.cm. of oxygen; the amount of oxygen that will combine with a sample of blood can be measured accurately and the hæmoglobin content of the sample thus estimated.

Another property is its iron content. Hæmoglobin has a known chemical formula in which there is one atom of iron, so that by estimating the amount of iron in the red cells from a given volume of blood it is possible to calculate the amount of hæmoglobin in the sample.

Hæmoglobin is a protein with a known refractometric index. By measuring this index it is possible to calculate the amount of hæmoglobin in any sample.

Yet another property of hæmoglobin is its colour and this can be measured in the various ways indicated below.

Whilst the property of hæmoglobin easiest to measure is its colour, the most fundamentally

important property is its oxygen-carrying capacity. There is evidence that these two properties are very closely correlated, so that if an instrument which measures the colour is first calibrated by the oxygen-carrying method a very close approximation of the hæmoglobin content of a sample can be obtained by the former method.

Most clinical hæmoglobinometers that are now sold are thus calibrated.

*Clinical methods of estimating hæmoglobin.*—Of the many methods of estimating hæmoglobin that are in use, none of the simpler methods is above criticism, while the more accurate procedures, e.g., van Slyke's oxygen-carrying-capacity method, are hardly suitable for general clinical practice. Most of the clinical procedures in common use are methods of measuring the colour of the hæmoglobin and are based on one or other of the following principles:—

I. Direct comparison of the colour of undiluted blood against a graduated colour standard.

(a) On special blotting-paper (Tallqvist).

(b) Between glass-plates (Dare).

II. Comparison of blood diluted to a fixed percentage against a graduated colour standard.

(a) Diluted with sodium carbonate solution and compared with a coloured-glass wedge (Fleischl-Miescher).

(b) Diluted with deci-normal hydrochloric acid and compared with a coloured-glass wedge (Hellige-Neoplan).

III. Comparison of blood diluted to a varying degree with a fixed colour standard.

(a) Diluted with water and compared to a permanent picocarmine standard (Gowers).

(b) Brought into contact with carbon monoxide, diluted with water, and compared with a permanent colour standard (Haldane).

(c) Diluted with deci-normal hydrochloric acid and compared with a permanent standard of acid hæmatin (Sahli), or a coloured glass block (Hellige).

IV. Comparison of blood diluted with deci-normal hydrochloric acid to a fixed percentage against a fixed colour standard in a colorimeter of the Duboscq type.

(a) Water placed in one chamber of the colorimeter and a standard coloured disc interposed (Newcomer).

(b) Compared with an acid hæmatin solution of known strength.

Other methods which require more elaborate instruments depend on the intensity rather than the colour of the light transmitted through hæmoglobin solutions; this is measured by means of a photo-electric cell.

In the writers' laboratory the new Hellige 'normal hæmometer' is used for all clinical purposes. The great advantage in the Hellige instrument is that it is possible to match the

brown-coloured acidulated blood solution with the colour standard exactly, and, as the standard is made of coloured glass, it is unlikely to undergo any colour change; one coloured prism which has been in use in our laboratory for more than four years has not undergone any colour change during this period. The sources of error, excluding those of carelessness in technique, using dirty pipettes, etc., will arise through variations in the diluting pipettes and in the calibres of the graduated tubes. The method suffers the disadvantage that with each dilution only one reading can be made—a second observer can check the reading, but not make an independent one—and that a time interval of fifteen to twenty minutes must be allowed before reading the result.

*Methods of expressing the results.*—The amount of hæmoglobin in an individual's blood may be expressed—

hæmoglobin in terms of a percentage of an unknown and arbitrary standard, and to adopt the first and express results in terms of grammes of dry hæmoglobin per 100 c.cm. of blood.

Instrument makers, who have hitherto made no attempt to adopt a universal standard, and hæmatologists, who have not encouraged them to do so, are both responsible for the present unsatisfactory state of affairs.

The confusion that exists cannot be better exemplified than by the table (I) below which shows that not only are there differences in the standard between instruments of various makes, but instruments of the same name made at different times vary from one another, and finally various authorities give different figures for apparently the same instruments.

However, many instruments that are now sold give the readings in terms of grammes of hæmoglobin per 100 c.cm. of blood; others give readings

TABLE I

*Amounts of hæmoglobin per 100 c.cm. of blood which are shown as 100 per cent by different instruments*

Authority	Tallqvist	Sahli	Dare	Newcomer	Haldane	Fleischl-Miescher
Pepper and Farley, 1933 ..	13.8	17.3	13.77 (old) 16.9 (new)	..	13.8	15.8
Nicholson, 1934 .. ..	15.8	17.2 (old) 14.5 (new)	13.8	16.9	..	..
Whitby and Britton, 1939 ..	13.8	17.3 (old)	15.9	..	13.8	..
Kracke and Garver, 1937 ..	15.8	17.3 (old) 13.8 (new)	13.77	16.9	..	..
Levinson and MacFate, 1937	15.8	17.3	16.0	15.92	..	..
Ordway, Gorham and Issacs, 1937.	15.8	13.8* to 17.2	13.7 to 16.0	16.9	13.8	15.8
Beck, 1938 .. ..	13.8	13.8* to 17.3	13.7* to 16.9	16.9	..	..

\* Different instruments are supplied with different standards.

(i) As the number of grammes per 100 c.cm. of blood, or (ii) as the percentage of the amount present in the blood of the 'normal' individual.

The disadvantage in the latter method is that there is no uniformity of opinion as to what is a 'normal' individual. Figures for the 'normal' given by different writers vary from 13.8 to 17.3 grammes, and in our personal experience we have found amongst groups of so-called healthy coolies in Assam a figure lower than the former, and amongst healthy Europeans in India one higher than the latter. If the expression '100 per cent hæmoglobin' has any meaning at all, it must imply that the particular sample is what one would expect from that individual if he were in perfect health. This would mean that a different standard would have to be adopted for each class of individual, a procedure which would lead to endless confusion. It is therefore better to abandon the second method, namely, that of giving the

in duplicate so that it is easy to see what corresponds to 100 per cent, or, if they use the older method, they state what their 100 per cent corresponds to in terms of dry hæmoglobin.

The excuse given for adhering to the older method (ii) is that most practitioners are familiar with this method of expressing the hæmoglobin. It may be true that they are familiar with the expression, say, 'hæmoglobin 80 per cent', but they don't know what it means, for it may mean anything between 11 and 13.8 grammes of hæmoglobin per 100 c.cm. of blood, a discrepancy which is far from negligible. They must therefore learn something new, so why should they not learn a new method which has a definite meaning accepted by all hæmatologists. Most American medical books are now using the 'new nomenclature' and in Great Britain the more conservative clinicians will follow the lead already given by British hæmatologist, in course of time.



A table (II), showing the 'normal' hæmoglobin levels in different populations in India with a few samples from other countries for comparison, is given below :—

are the coloured prisms in the front and an opaque glass plate at the back. Through a hole in the housing the mixing tube is introduced and lies at the

TABLE II  
'Normal' hæmoglobin levels of different populations

Sex	Age	Locality	Economic status	Hæmoglobin in grammes per 100 c.cm.	Standard deviation	Number on which based	Authority
Males	19-30	Bombay	Students	15.37	$\pm 0.96$	121	Sokhey <i>et al.</i> , 1937.
	25-45	Calcutta	Mixed, servants.	14.77	$\pm 1.36$	50	Napier and Das Gupta, 1935a.
	25-45	"	Clerks and doctors.	15.70	$\pm 0.91$	30	" " " 1936.
	Adults	Assam	Coolies	12.63	$\pm 1.41$	20	" " " 1936.
	"	Cachar	"	12.60	$\pm 1.83$	25	Napier and Majumdar, 1938.
	"	Assam	"	11.83	$\pm 1.67$	24	Napier and Das Gupta, 1935b.
	"	Shivrajpur	"	13.74	$\pm 1.79$	47	Sen (Napier, 1939).
	"	"	"	12.95	$\pm 1.72$	49	" ( " ).
	"	U. S. A.	"	16.00	..	..	Castle and Minot, 1936.
	"	Britain	"	15.60	..	..	Whitby and Britton, 1939.
Females	18-30	Bombay	"	14.50	..	..	Price-Jones, 1931.
	14-38	Calcutta	Middle class	12.99	$\pm 1.10$	101	Sokhey <i>et al.</i> , 1938.
	17-22	Madras	Students	12.63	$\pm 1.01$	128	Napier, 1939.
	17-30	Delhi	Middle class	13.73	$\pm 0.93$	62	Sankaran and Rajagopal, 1938.
	Child bearing.	Coonoor (6,000 feet).	"	13.11	$\pm 0.81$	100	Benjamin, 1939.
		"	"	15.81	$\pm 2.54$	100	Radhakrishna Rao, 1938.
		Cachar	Coolies	10.40	$\pm 1.74$	25	Napier and Majumdar, 1938.
		Assam	"	10.80	$\pm 2.30$	20	Napier and Bilimoria, 1937.
	"	Britain	"	13.60	..	..	Price-Jones, 1931.
	18-22	Michigan	Students	13.70	..	..	Whitby and Britton, 1939.
				13.76	..	50	Bethell, 1936.

#### Hellige normal hæmometer

The instrument consists of the following parts :—

- (i) A mixing tube with graduations from 10 to 170 (see figure, A).
- (ii) A pipette with a mark at 20 c.mm. capacity (B).

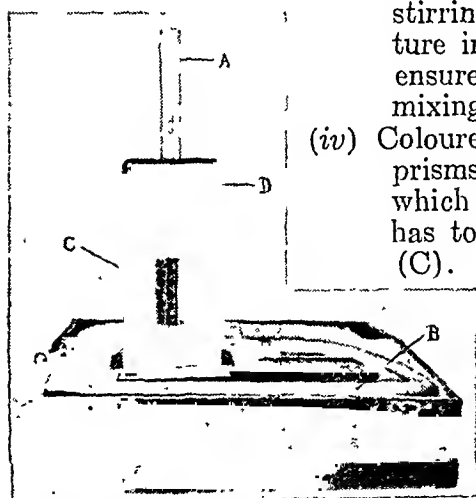


Fig.—Hellige normal hæmometer.

- (v) The housing of the hæmometer (D) which is made of steel with a large base to ensure safe standing. Inside the housing

same distance from the eye as the prism.

**Technique.**—Fill the graduated measuring tube up to mark 10 (using a large pipette) with N/10 hydrochloric acid.

After shaking the blood in the flask for three minutes, with the pipette draw up the blood to the 20 c.mm. mark exactly, wipe away any blood adhering to the outside of the pipette, and transfer the blood into the measuring tube. If the blood goes a little beyond the mark, it is brought back to the mark by touching one's finger with the tip of the pipette a few times.

By repeated filling and emptying the pipette should be completely freed from all vestiges of blood, and the blood should be intimately mixed with the hydrochloric acid; the red hæmoglobin now turns to acid hæmatin (brown).

Wait for fifteen to twenty minutes; the mixture which is now brown should be perfectly clear.

Now add water slowly drop by drop with a pipette, mixing constantly with the solid glass rod, until the mixture matches exactly the colour of the standard prism C in the housing. During the process the solid rod should not be placed on the table, as each time it is allowed to touch anything the small amount of mixture adhering to the rod will be lost, and this source of error will be multiplied.

To match the solution and the standard, the hæmometer should be held up to a good source of indirect natural light, direct sun-light and artificial light being avoided. The level in the mixing tube opposite the lowest point of the meniscus of the diluted acid hæmatin is read; this gives the percentage of hæmoglobin. The end point is generally very sharp and there is seldom any difficulty in matching the solution and standards exactly, except with leukæmic and jaundiced blood. When a point is reached at which the solution appears to match the standards, take a reading; then add a drop of water, mix the solution, hold up to the light and take a second reading. If at the second reading the solution is definitely too light the first reading should be taken. On the other hand if the second reading still appears to match the standards, but, after yet another drop has been added, the solution is definitely lighter than the standards, the result should be the mean of the first two readings.

The present writers, Napier and Das Gupta (1935), calculated that 100 per cent with the Hellige normal hæmometer represented 13.67 grammes by the refractometer method, but later by means of the van Slyke oxygen-carrying method a slightly higher figure was obtained and they decided to consider 100 per cent as 13.75 grammes.

Other instruments of this pattern (Hellige normal hæmometer) that they have used have not differed appreciably from this standard, but it is advisable to have the colour standard with the pipettes and mixing tubes to be used, tested in some laboratory where the van Slyke oxygen-carrying method is also employed.

The reading in terms of percentage from the tube must be converted into grammes; this can be done conveniently by using the conversion table of which the skeleton is given below (table III). It is recommended that the full table be prepared and kept handy.

TABLE III

*Skeleton table of hæmoglobin values of the Hellige normal hæmometer converted into grammes of hæmoglobin per 100 c.cm. of blood*

Per cent Hellige	Grammes per 100 c.cm.	Per cent Hellige	Grammes per 100 c.cm.
1	0.1375	10	1.375
2	0.2750	20	2.750
3	0.4125	30	4.125
4	0.5500	40	5.500
5	0.6875	50	6.875
6	0.8250	60	8.250
7	0.9625	70	9.625
8	1.1000	80	11.000
9	1.2375	90	12.375

100 per cent Hellige = 13.75 grammes per 100 c.cm.

(Continued at foot of next column)

## THE NEEDLE IN THE VEIN

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THE intention is to discuss ways of entering as well as of avoiding a vein, and also to comment on the sterility of the implement used.

1. *Should the vein be entered by a primary thrust, from above, through the skin and the wall of the vein together, or by a secondary thrust, from above or from one side, after the skin has been traversed?*

The trauma is minimum when the primary thrust is made from above, through the skin and

(Continued from previous column)

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the wall of the vein together. This procedure is possible when the vein is fixed either naturally or by the finger of the operator.

If the needle has traversed the skin and then travelled between the skin and the vein or to one side of the vein, it can be made to enter the vein by a secondary thrust from above or from one side. The secondary thrust being more oblique than the primary one has a more tearing action. The trauma is greater. The procedure of choice, therefore, is the entry with a primary thrust from above.

## 2. Should the oblique opening in the needle be upwards or downwards?

The needle has a cutting edge (not a boring point) and takes a flap from the wall of the vein into the lumen. In figure 1 the needle is introduced into the vein of the arm, pointing towards

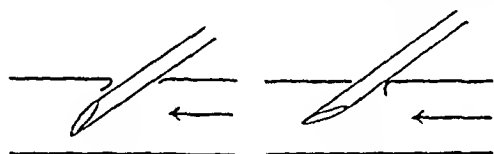


Fig. 1.

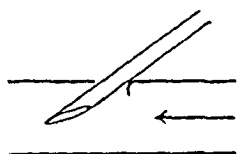


Fig. 2.

the heart as is done in giving an intravenous injection, with the opening looking upwards. The flap is bent with its *convexity* against the flow of blood (indicated by the arrow). On withdrawal of the needle such a flap may not fall back into position easily. In figure 2 the needle is introduced in the same direction but with its opening looking downwards. The flap is bent with its *concavity* against the flow of blood. On withdrawal of the needle such a flap will fall back into position easily. If the needle happens to puncture a valve in the vein the consideration for the flap acquires added force.

In giving an injection the introduction of the needle pointing towards the heart, apart from directing the injected fluid centrally, enables the operator to face the subject and watch the latter's face. In taking blood from a vein it might be thought that the needle should be introduced pointing away from the heart and that the oblique opening should look upwards. There is, however, no need to introduce the needle pointing away from the heart and lose the benefit of watching the subject's face. With appropriate compression on the limb (not abolishing the pulse) the blood in the vein, being under pressure, flows regardless of the direction of the needle.

It has been recommended (Wiener, 1935) that in dealing with small veins the needle may be introduced pointing away from the heart. It does not appear to be necessary to do this. The procedure of choice, therefore, is the introduction of the needle pointing towards the heart with the oblique opening looking downwards.

## 3. The bore of the needle

The writer in a recent communication suggested that the bore of the needle for taking

blood from a vein for transfusion should not be larger than that of a 20 c.cm. Record syringe needle which is usually used in giving intravenous injections (Grevall and Chandra, 1940). Since then other workers' opinion to the same effect has become available (Boland, Craig and Jacobs, 1939, publication delayed in transit).

## 4. Special sites for puncture when the needle has failed to enter a vein at the usual sites

Attention is drawn to three special sites: (i) for taking blood or giving an injection veins over the malleoli are available regardless of the obesity of the subject; (ii) in small children the external jugular vein can be entered; and (iii) for giving saline or blood, corpora cavernosa of the penis (Snyder, 1929) can always be entered.

A puncture in the fontanelle in infants is to be avoided.

## 5. How unintentional entry into a vein can be avoided

(1) When giving an intramuscular injection, the needle should first be introduced and a dry puncture assured. The syringe containing the medicament is then attached to the needle. When the medicament is contained in a rubber-capped bottle, yet another needle suitably stuffed with sterile cotton-wool is necessary to admit air (filtered) into the bottle, to replace the volume drawn into the syringe.

(2) When giving a subcutaneous injection needing speed, as is done in antirabies clinics, and involving regions which cannot be guaranteed to be free from venules, such as the abdominal region, it is better not to use a fine needle. The chances of a needle with a large bore, such as is used with a 20 c.cm. Record syringe needle, of entering a venule are much less than those of a fine needle.

(3) When giving a subcutaneous injection in the arm, pinching the skin and inserting the needle in the base of the fold are to be preferred to stretching the skin and thrusting the needle into it. In the tissue over which the skin is stretched venules are flattened and are likely to be entered by a fine needle which is usually used. In the tissue which is pinched the venules are stretched and narrowed. They are more likely to be cut across than entered by even a fine needle. Even for this injection the writer does not use a fine needle.

## 6. Sterility of the needle

Sterility of the syringe was discussed in no less than nine communications, in the *British Medical Journal*, between 30th April, 1938 and 11th June, 1938—i. Editorial Annotation (1938), ii. Crabbe (1938), iii. Murray (1938), iv. Jones (1938), v. Smalley (1938), vi. Editorial Comment (1938), vii. Gray (1938), viii. Manclark (1938), and ix. Pines (1938). It came up again as an integral part of a review of recent advances in vaccine therapy, in 1939 (Fleming,

1939). The present writer adds the observation that a syringe and needle, howsoever sterilized, cease to be sterile when dried by sucking and expelling the ordinary air of the room. He generally uses a Record syringe and his method of sterilizing is to : (i) clean the syringe and the needle immediately after use, (ii) leave them for 15 minutes in 7 per cent phenol in water, (iii) transfer them to a pan of boiled water, (iv) dehydrate them by sucking and expelling absolute alcohol—second quality, kept for the purpose, (v) keep them assembled ready for use, in absolute alcohol in metal cases and (vi) wash them by sucking and expelling sterile saline. Once a month the metal containers are emptied into a jar to yield the absolute alcohol of the second quality and refilled. The absolute alcohol of the second quality is also renewed once a month. When a Roux's syringe is used, it is sterilized every day in hot oil (temperature 120° to 140°C.) completely to begin with, *i.e.*, all the parts excepting the top of the rod of the piston are dipped separately and then assembled. Later, filling the syringe and the needle twice with the oil suffices. Excess of oil is removed (if desired) by sucking air through a flame (for this step a guard covers the needle) and expelling it, or preferably by sucking and expelling boiling water.

#### 7. *Prepuncture and postpuncture care of the skin, the vein and the subject*

Painting liberally with simple solution of iodine (*B. P.*) is preferable to swabbing with spirit or a solution of phenol. The stain is removed (if desired) by swabbing with absolute alcohol. Immediately before the withdrawal of the needle compression on the limb is removed and a swab (on a stick) soaked in the iodine solution is placed in contact with the needle to press on the puncture the moment the needle is withdrawn. Bleeding, if any, is checked by pressure. Flexible collodion (*B. P.*) is dropped on the puncture with a dropper to cover an area the size of the thumb nail. After a false skin has formed (which may be delayed in hot and wet months for over 15 minutes) the subject is allowed to depart with advice that the punctured limb should not be used in exertion of any kind for 24 hours.

Prepuncture care is specially important when the subject is a donor of *blood for cold storage*. The fact that accidents never (or hardly ever) occur with the therapeutic use of the needle, after a certain precaution has been taken, does not guarantee the bacteriological sterility necessary in storing blood. Stray micro-organisms injected into the blood stream of living subjects are as a rule promptly destroyed; injected subcutaneously they are also destroyed with some effort on the part of the tissues; swept into blood taken for storage they may or may not be overwhelmed; falling into culture media they will grow as contaminants without fail, of course. Liberties taken with the needle in therapeutical

procedures will more often than not contaminate nutrient broth and agar. The same remarks apply to the syringe.

Incidentally, the syringe and needle which are filled with ordinary air in order to replace the contents of a rubber-capped bottle are not, strictly speaking, sterile although they are more so than when they have been dried by repeated filling with air. Sterility of the contents of a rubber-capped bottle into which have been blown many syringes full of unfiltered air is always doubtful.

The swabs on sticks are sterilized and kept in separate test tubes.

The subject, if a donor for cold storage, should attend after a very light meal, if not after only liquid refreshment. Chyle in the blood interferes with the examination of the contents of the stored bottle. He should be accommodated in a long chair in which he can be placed in a supine position if necessary. Aromatic spirits of ammonia (*B. P.*) and drinking water should be available. Means of applying pressure over a hæmatoma should also be available. Provision must also be made for dealing with hæmophiliacs.

#### 8. *Importance of minor details*

The long list of recent references appended to this short communication is indicative of the importance of the items concerning which minor details have been given. More veins have been pricked in England and India during 1939 than ever before. The practice is likely to last. It is hoped that these remarks on minor details will add to the ease, safety and utility of the process of pricking veins and tissues.

#### *Summary*

1. A vein is best entered by a primary thrust from above, through the skin and wall of the vein together.
2. The needle should be directed towards the heart with its oblique opening downwards.
3. A needle of large bore should not be used for taking blood.
4. When for any reason a needle cannot enter a vein at the usual sites, other useful sites for injection are : (i) veins over the malleoli, (ii) external jugular vein—in small children, and (iii) corpora cavernosa of the penis. The first two sites serve for taking blood also.
5. Entry into a vein has to be avoided in giving injections subcutaneously and intramuscularly. For the former the needle should not be extremely fine and the skin should not be stretched, but pinched. For the latter the needle must be introduced alone and a dry puncture assured.
6. A long list of recent references on sterility of the syringe (and of necessity of the attached needle) is available. An additional observation is that the syringe and needle dried by sucking and expelling air from a room are not sterile.

7. Prepuncture and postpuncture care of the skin and the vein are best assured by iodine before and collodion and rest after the puncture. Drinking water and aromatic spirits of ammonia should be at hand, and so should be the means of stopping bleeding from the puncture.

8. Minor details in pricking veins and tissues have become more important recently.

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### SUMMARIES OF THE PAPERS READ AND THE DISCUSSIONS THAT FOLLOWED, AT THE TUBERCULOSIS WORKERS' CONFERENCE, NEW DELHI, 20TH TO 23RD NOVEMBER, 1939

#### A. DIAGNOSTIC METHODS

##### (a) 'X-ray as a Guide to Diagnosis' paper by Dr. T. J. Joseph

WHILE it is not true that x-rays are everything, it cannot be denied that tuberculosis work done without their help is bound to be unsatisfactory. In a national campaign against tuberculosis facilities for early diagnosis by x-rays are essential, both if the disease is to be cured in the individual and if it is to be prevented in the community.

X-ray examination has its limitations and pitfalls and it cannot completely cover blanks left by clinical laziness. Various devices like careful screening, stereoscopy, serioscopy, tomography, etc., are now used to overcome limitations arising out of the anatomical position of the lungs and the lesions. Special reference was made to the hilus region as the most common area for mistaken diagnosis.

Fluoroscopy has its obvious advantages but it is only complementary to other procedures and not an alternative to radiography.

##### (b) 'Physical Examination and Clinical Observation as a Guide' paper by Dr. L. R. Dongrey

In emphasizing the importance of x-ray for early diagnosis a slogan has been evolved that 'tuberculosis must be seen and not heard'. When it is known that x-ray examination has its limitations and pitfalls, such a tendency shows lack of correct perspective. The objective of the clinician is to study the patient and his reactions to the disease as expressed in his symptomatology. As the early symptoms are often vague and elusive and may be common to several diseases a period of close and prolonged observation of the clinical course of the disease is essential.

Physical signs express the physical condition of the subjacent viscera, but do not indicate the aetiology of the signs nor always give information about the activity of the underlying disease. Physical signs derive their value in association with symptoms. Of all methods of physical examination auscultation is the

most reliable, and the most reliable of all auscultatory signs when obtained is persistent râles over the upper portion of the lungs. This is almost diagnostic of pulmonary tuberculosis provided suggestive symptoms are present.

The clinical study of the signs and symptoms makes the diagnosis probable, the laboratory may confirm it as well as the x-ray.

##### (c) 'Blood Examinations and Examination for Tubercle Bacilli as a Guide' paper by Rev. R. M. Barton

Examinations for tubercle bacilli are the most important. The methods aimed at are those which provide the highest possibility of finding bacilli which are present, avoiding those which give false positives.

Culture of bacilli is now possible in all fairly well-equipped laboratories and Jensen's modification of Lowenstein's medium is widely used. If sufficient material is seeded, this method gives equally good and sometimes superior results to that of guinea-pig inoculation, which is expensive and takes longer than the culture method.

Figures from 1,200 consecutive cases from the Union Mission Tuberculosis Sanatorium, Arogyavaram, are given and a plea is made for the adoption of minimum standards with regard to positive and negative findings on admission to, and discharge of a patient from, the institutions. The aim of all institutions should be to include sputum and stomach-wash cultures, and it is suggested also that certain laboratories should be entrusted with research work with regard to the bovine and human type of infection in India for which very little work has been done so far.

No blood picture specific for tuberculosis has yet been found. Examinations for changes in the leucocytes and sedimentation rates are commonly used. These have to be used with caution for positive diagnosis, as their main value as regards diagnosis up till now is only in excluding active tuberculosis.

##### (d) 'Tuberculin Test' paper by Dr. P. K. Sen

The specificity of this test has recently been contested by few workers, but for practical purposes the test can be accepted as specific by denoting infection with tubercle bacilli. Various methods of the test are mentioned but the Mantoux method is considered to be the most valuable and is preferred. In order to obtain uniform results only induration should be taken into account in reading the results of the test, and not erythema.

As higher doses make the test non-specific, doses bigger than 1 mg. are not recommended. Negative reactions, with certain limitations, exclude tuberculosis, and with positive reactions the younger the subject, the stronger the chances of active disease being present.

#### Discussion

In discussion, the importance of x-ray examination in diagnosis was emphasized, including tomography, and was thought by many to be the most important of all the methods of diagnosis. At the same time others emphasized physical examination and the observation of clinical symptoms, and considered those equally important. With regard to x-ray, there was a general desire for some kind of standardization of the terms used in describing abnormalities in the radiograph. The necessity for research as to whether bovine tuberculosis is present to any extent in India, was brought out.

The result of the discussion was that the difficulty of diagnosis was realized and that frequently diagnosis could not be made by using one method alone, but that all the facts provided by x-ray examination, physical examination, laboratory examination, and a study of clinical symptoms, were often needed, before a final diagnosis could be made.

#### B. 'IMMUNO-BIOLOGICAL DEFENCE MECHANISM' BY DR. C. FRIMODT-MÖLLER

Difference of opinion exists about the relationship of allergy and immunity to each other, and about their



individual rôle in the healing of tuberculous lesions. The allergic reaction fixes the bacilli to the seat of implantation by an exudative inflammation, which also diminishes the flow of lymph into the body from the lesions, and thereby also checks the flow of toxins into the general circulation. Further, the response of the body leads to the production of various bodies which confer a relative immunity against re-infection. But should a re-infection occur, due either to a too massive re-infection or to too virulent bacilli, the local defence mechanism may act so severely that the very defence measure becomes destructive and very dangerous to the patient himself, in its attempt to eliminate the lesions in the lungs.

The special treatment of pulmonary tuberculosis, therefore, aims at a careful regulation of the action of the immuno-biological defence mechanism so that on the one hand it does not act too strongly, and on the other hand acts strongly enough to produce gradual and solid healing of the lesions. Physical and mental rest, and sometimes localized rest of the diseased part by various surgical procedures, are the means of influencing the defence mechanism favourably. The special treatment, therefore, consists of rest and graded exercise in the right proportion in each individual patient so that enough tuberculo-proteins are allowed to circulate in the blood, but only enough to create an inflammatory exudation sufficient to build up strong scar-tissue round the foci and so produce a lasting healing.

#### C. METHODS OF CONTROL OF THE TREATMENT

##### (a) 'X-Ray as a Guide to Treatment' paper by Dr. P. V. Benjamin

A cursory examination of the film is sufficient for diagnosis, but a detailed study is necessary for judging the line of treatment; the extent, distribution, type and character of the lesion; the number, location and the nature of the walls of cavities when present; and the position of the mediastinum. The condition of the diaphragm and pleura can only be judged by an x-ray film and a careful fluoroscopy.

It is being realized that routine examination is incomplete without an x-ray examination and this applies equally to initial and subsequent examinations. Institutions are therefore now planned where examination rooms and x-ray rooms form one unit. In taking serial films, the various films should have as far as possible equal exposures, otherwise they may create false impressions.

##### (b) Paper on 'Clinical Observation as a Guide to Treatment' by R. B. Dr. Kesava Pai and Dr. Jay Ram Naidu

Pulmonary tuberculosis is a highly pleomorphic disease. No two cases are identical; therefore, a close clinical observation of the progress of the case is as important as x-ray and laboratory tests. A normal pulse rate and temperature does not necessarily indicate inactivity of the disease. General condition, pulse rate differences between daily maximum and minimum temperatures, sedimentation test, blood index and results of physical examination may each and all be helpful in judging activity.

Clinical observations, often, though not always, give timely indication for necessary changes in the line of treatment.

##### (c) Papers on 'Physical Examination as a Guide to Treatment' by Drs. P. T. Patel and C. N. Chandrachud

While admitting the limitations of the value of individual physical signs, it must be stressed that a thorough methodical physical examination can give valuable information to the clinician. It indicates the rough structural changes that have taken place in the underlying organs, but these findings to be of real help must be compared and correlated with information supplied by other methods.

##### (d) 'Blood Examinations as a Guide to Treatment' paper by the Rev. R. M. Barton

The quick response of the blood picture to changes in the patients' condition makes it a valuable guide during treatment, especially so as these, generally speaking, precede the clinical symptoms.

The importance of leucocytic reaction and sedimentation rate is emphasized. A blood index based on (1) the neutrophile-lymphocyte ratio, (2) the mononuclear-lymphocyte ratio, (3) the percentage of neutrophiles of Stabkernige form and (4) the percentage of Westergren one-hour sedimentation reading, has been used for the last seven years at the Madanapalle Sanatorium and has served as a valuable guide in assessing the condition of the patient under ordinary sanatorium treatment.

Adverse changes in the blood indicate either some complication, or the spread of the disease in the diseased or the contralateral lung or may suggest that too much exercise is being done. But to be of real value blood examinations must be made at regular intervals, and be made by experienced blood workers.

#### Discussion

In discussion following the papers, several speakers stressed the importance of control of treatment by x-ray, although it was recognized that frequent x-ray examination of patients was not always possible for the general practitioner. A number of speakers showed also how important clinical observation and physical examination were, in addition to x-ray examination, and several spoke of the value of blood examinations. As in diagnosis, so in control of treatment, one method alone was insufficient, and if the patient was to get the best treatment x-ray examination, physical examination, blood examination, and observation of clinical symptoms, must all be employed.

#### D. TREATMENT

##### (a) 'Artificial Pneumothorax' paper by Dr. D. V. Muthu

Nowadays nobody questions the value of collapse therapy or the merits of the underlying principles, though there is slight diversity of opinion as to how soon it should be employed in an individual case. Decision should be made taking into account the history of the case, the course of the disease, and its character, as revealed by examinations and constitutional symptoms.

Indications for artificial pneumothorax are mentioned. As this operation in a great majority of cases makes a patient free from tubercle bacilli it assumes extra importance for public health reasons. It also reduces the stay of the patient in a sanatorium and enables him to return to work early and it has therefore a great social value.

##### (b) 'Thoracoscopy' paper by Dr. P. V. Benjamin

Artificial pneumothorax is not successful in every case and 40 per cent of its failures are due to adhesions, which are often distributed over the diseased part of the lung making a selective collapse impossible.

Two types of thoroscopes are described and the advantages and disadvantages of diathermy and galvanocautery are discussed and the difficulties of cutting adhesions in certain situations are brought out.

A recent acute onset is a contra-indication to the operation. A complication after the operation is pleural effusion, but its frequency is not more than in artificial pneumothorax.

Review of the results of 210 operations in 186 patients at the Madanapalle Sanatorium shows that by artificial pneumothorax 53.5 per cent of the patients became bacilli free, whereas the figures after cauterization of adhesions were 63.7 per cent. The operation, therefore, improves the expectation of life and saves many a patient from serious operations like thoracoplasty.

##### (c) 'Thoracoplasty' paper by Dr. W. G. Jones

It is emphasized that it is an error to adopt this operation:



considered to be too drastic and therefore too dangerous for Indian patients, while it is no less an error to consider it to be so easy as to suppose that every surgeon can perform it. This operation needs to be known and used in India more than it is at present. Its risks are small with skilled and experienced surgeons, and it offers considerable chances of cure to that large group of cases that cannot benefit by pneumothorax or phrenic surgery. While its application is chiefly to unilateral cases, it can be used in conjunction with contra-lateral pneumothorax and phrenic interruption in many bilateral cases as well. To most, if not to all, chronic cases in which pneumothorax has failed, thoracoplasty offers the shortest road to cure and a good proportion can be rehabilitated for work.

(d) 'Phrenic Nerve Operations' paper by  
Dr. R. Viswanathan

These are used to produce temporary or permanent paralysis of the hemi-diaphragm. It is a component procedure in the armamentarium of collapse therapy. It has its limitations and the results will depend on the judgment exercised in its application. Various indications for the operation are mentioned. A modified technique for the operation with the patient sitting in a dental chair is recommended.

*Discussion.*

*Surgical treatment.*—In discussion, several spoke of complications in artificial pneumothorax treatment, and some described the apparatus, which they are using, designed to avoid some of the accidents possible in giving artificial pneumothorax. In home treatment of tuberculosis, too, artificial pneumothorax had to have a place, because early treatment and prevention of spread of infection were urgent, and a simple apparatus was necessary for this. Some discussion took place on aspiration of pleural fluid and replacement by air. Hæmoptysis following artificial pneumothorax was mentioned by several.

In the discussion of thoracoscopy, the advantages and disadvantages of the direct and indirect vision type of apparatus were brought out; the complication of subcutaneous emphysema, the question of cauterizing adhesions which did not keep open a cavity and when the sputum had become negative, and the control of subsequent refills by x-ray were also raised.

In the discussion on phrenic operations, the general consensus of opinion was against phrenic operations as the operation of choice; there was a risk of irresponsible operation just for the sake of doing something and because it was an easy operation. It still had a place in a small number of cases in which other measures had failed. Some discussion took place on the position of the patient during operation—sitting up or lying down.

*Thoracoplasty.*—In a vigorous discussion there was criticism of Dr. Jones' opening paper, some speakers not agreeing that the percentage of patients in whom thoracoplasty was indicated was as high as that suggested in the paper; some considering there was an over-emphasis on surgical methods as against non-surgical methods of treatment of pulmonary tuberculosis. In reply, Dr. Jones stated that the aim in treatment was to use methods which produced the best results, and he believed that in a large number of patients it was proved that thoracoplasty did do this.

(e) 'Gold Treatment' paper by Dr. Y. G. Shrikhande

While a good deal has been said for or against the use of gold, the fact that it is still used is evidence of its efficacy in suitable cases. Of the various preparations in the market the choice lies between sanocrysin and solganol.

Gold treatment is of special value in exudative lesions, but in selecting cases attention should be paid to the extent of the disease, resistance of the patient and efficacy of his eliminative mechanism. While large doses are harmful, smaller doses are useless and a plan for proper dosage is suggested.

Intra-pleural injections of gold salts with repeated aspirations have also been used with good results in the treatment of pleural effusions complicating pulmonary tuberculosis.

*Discussion*

The question of treatment with gold preparations evoked much discussion, some maintaining that there was little evidence of its producing any good results, others maintaining that after a considerable experience over many years they were convinced that it was of value, especially in fresh exudative lesions and as an aid in controlling disease in the contra-lateral lung during artificial pneumothorax treatment. Dosage and complications, and contra-indications, were discussed.

At the end of the discussion the question of carbolic injection was raised and the experience of those who had tried it was against continuing this treatment, as also with cadmium sulphite.

E. 'PROGNOSIS AND AFTER-RESULTS' BY  
DR. P. V. BENJAMIN

It is pointed out that in the general population the prognosis of tuberculosis is good, but in an individual in whom the disease has become manifest a great many factors—age, sex, type of the disease, presence of tubercle bacilli, complications both tuberculous and non-tuberculous—have to be considered. The influence of an early diagnosis, appropriate treatment, and proper after-care cannot be over-estimated.

Figures for the after-results of patients discharged from different sanatoria are given and show improved prognosis under modern methods of treatment.

*Discussion*

A short discussion served mainly to emphasize what was already in the paper, together with some mention of family history, nutrition, and the question of urban and rural origin.

F. 'CLASSIFICATION OF STAGES OF PULMONARY TUBERCULOSIS AND OF "DISCHARGE" RESULTS' BY DR. A. C. UKIL

An intelligent basis of classification is not only useful in assessing prognosis and in advising treatment, but essential in comparing results of different methods of treatment followed by workers in different institutions in the country.

With modern advances in the methods of diagnosis and assessing prognosis, different countries have adopted different types of groupings, which are more or less amplification of the Turban-Gerhardt classification.

Information collected in India shows that except the Madanapalle group of sanatoria, no two institutions followed any uniform standard. Discrepancies in the criteria followed by different institutions are pointed out in the paper.

A classification of the adult type of pulmonary tuberculosis based on radiological extent of the disease is suggested.

*Discussion*

The difficulty and at the same time the necessity of some standardizing of the classification of case records was well brought out in the discussion which followed the paper. A simple method of classifying the condition of the patient on admission and also on discharge were both required, as too detailed a classification would only lead to greater difficulty in standardization and comparability of records.

G. 'CAUSATIVE FACTORS IN THE DEVELOPMENT OF TUBERCULOSIS DISEASE' BY DR. B. K. SIKAND

The factors which turn infection into disease and also those which determine the course of the disease in a particular individual are not all well understood. Detailed surveys over a large number of areas and for prolonged periods can alone supply the information.

Absence of bovine infection in India is pointed out and the effects of race, age and sex on the incidence

of disease are discussed. Environmental conditions, the effect of bad housing and poor nutrition as causative factors are stressed. Bad housing and the unhygienic habits of the people provide the ideal condition for massive dose infection. Defective nutrition both in quality and quantity which is well known in India by its pauperizing action on the human physiology may represent a real tubercularizing agent.

#### Discussion

In discussion, the multitude of causative factors raised, only showed how little is really known as to what are the real factors in the spread of tuberculosis. One factor seemed certain, an open case *plus* overcrowding.

#### H. 'SPREAD OF INFECTION AND ITS PREVENTION' BY DR. K. S. SANJIVI

In the Western countries the campaign against tuberculosis is fought on two points—bovine and human sources. Absence of bovine infection in India is mentioned by some workers, but the number of studies on bovine infection is totally inadequate to warrant any dogmatic assertion. The human type of infection spreads mainly through the sputum. The infection may be direct, or indirect, through dust, flies, food and utensils.

Exogenous infection is now believed to play a more important rôle in the adult type of the disease. The open case must therefore be the focus of our attention, both in his own interest and in the interest of the community. An intensive search for open cases should therefore be organized and the aim of all treatment should be to render open cases bacilli-free.

Importance of co-operation of the general practitioner, the public health department, and tuberculosis hospitals in finding open cases and detecting contacts with early signs is stressed. Figures from Madras are given where, with the co-operation of the public health department, 81.3 per cent of the contacts of known cases have been examined.

#### Discussion

Discussion tended to deal mostly with the question of infection in institutions and specially among the staff of institutions treating tuberculous patients. Regular examination of nurses and doctors and others in contact with patients was recommended, but the use of masks suggested by some was not generally accepted.

#### I. 'TUBERCULOSIS CLINIC' BY DR. K. VASUDEVA RAO

A tuberculosis clinic is the pivot of an anti-tuberculosis scheme and the clinics should be scattered throughout the country—a clinic for every 50,000 of the population. These should be located in the crowded areas of the city. The building should be simple and all facilities for x-ray and bacteriological investigations should be available. The functions of the clinic in regard to diagnosis, treatment of cases, contact examination, and as centres for care and after-care and for education and propaganda, are discussed. The strength and the duties of the staff are described and a budget estimate for the recurring and non-recurring expenses of a clinic is given.

#### Discussion

A short discussion centred mostly on tuberculosis health visitors, their training, their work, and the number needed.

#### J. 'THE WORK OF THE CARE AND AFTER-CARE COMMITTEE' BY DR. T. J. MANI

Work of the care and after-care committee at Bangalore is described and compared with schemes in other countries. The Bangalore committee has made provisions to help needy patients with diet and special medicine, though this is not ideal, it is the best that can be done in the absence of sufficient hospital accommodation. As regards employment of arrested

cases a small factory where patients can work under medical supervision is advocated. As regards the care of infants, institutional separation is the one adopted in Bangalore, because familial boarding may not work satisfactorily. Preventoria for older children are necessary, but the financial position does not permit a move in this direction.

#### K. 'EX-PATIENTS' COLONIES' BY THE REV. R. M. BARTON

The success of modern methods of treatment of tuberculosis has raised many new problems. No doubt lives of many patients are prolonged but so is also the infectiveness of many of them, because the treatment in many patients does not produce permanent arrest or cure. An early return to unsuitable work and unhygienic surroundings not only leads to frequent relapses, but is dangerous to the family and the associates of the patients. In order to produce the best results both from the individual, and from the community's point of view, an individual who is permanently damaged by tuberculosis must be able to live and work in a sympathetic and happy atmosphere, under a disciplined freedom and with a suitable employment that provides security to the patient and his family and in a place where he knows that he can get help whether in health or sickness.

Reference is made to several schemes of after-care and rehabilitation in the Western countries, and the main principles on which the famous Papworth Village Settlement scheme is based are mentioned.

The activities and the growth of the Panipuram ex-patients' colony at Arogyavaram near Madanapalle where at present 12 patients (two with families) are living are described. Attention is drawn to the importance of proper selection of cases, and the correct choice of the industries.

#### Discussion

The necessity for care and after-care committees was agreed upon, as also ex-patients' colonies, but doubts were expressed by some in discussion whether managing bodies of institutions could be convinced of the need, or if money could be found; suggestions were also made of various possibilities for colonies. But if the need is recognized by the leaders in tuberculosis work, and they had vision and enthusiasm, there seemed no reason why colonies should not be established but they must be built in connection with treatment institutions.

#### L. 'INSTITUTION AND HOME TREATMENT' PAPERS BY DR. R. H. H. GOHEEN AND DR. R. K. KACKER

The vast majority of those afflicted with tuberculosis are found in their homes. This will continue to be true even when a large number of institutions representing various links in the chain of a complete anti-tuberculosis scheme are established. Home treatment therefore assumes a rôle which cannot be over-estimated. This can, however, only be provided with the co-operation of the general practitioner, who should be adequately instructed in regard to the methods of early diagnosis, treatment and of protection of contacts. He should be able to adapt an average home for proper segregation and should judiciously and tactfully effect a change in the patient's and family's dietary, which is very often unbalanced on account of ignorance of the correct facts. In fact, the entire economy of the patients has to be safeguarded.

Need for co-ordination of home treatment with institutional treatment is stressed. Of the many functions of sanatoria, their importance as training centres for doctors and centres for propaganda is emphasized.

#### M. 'TUBERCULOSIS SURVEY' BY MAJOR G. F. TAYLOR

Brief summary of tuberculosis surveys done in India is given and main conclusions which can be drawn from these surveys are mentioned. A plea for surveys all over India was made, as these not only help to define the extent and nature of the problem and of the causes of the spread of the disease in the community, but are useful also in detecting open cases.

Survey work is moreover an effective educational measure, as it awakens and directs public opinion to the problem and opens the way for proper legislative measures.

#### Discussion

In discussion, further information was given of surveys in different parts of India, of experience with tuberculin which had lost its potency, and of the dangers of using a 1 in 100 dilution in routine surveys. The necessity of tuberculosis clinics being properly staffed so that they could carry out surveys, was emphasized. Some discussion took place also on the type of disease as found by examination of patients and at post-mortem examination.

#### N. 'PROPAGANDA AND EDUCATIONAL CAMPAIGN' BY DR. A. R. MEHTA

Ignorance about everything scientific is too well known in India but the ignorance about the causes and methods of prevention of tuberculosis is colossal; and if there is any one weapon which can be of greatest use in the fight against the disease, it is the educational campaign.

The broad principles of educational campaigns are mentioned and it is emphasized that attention should be focused on the child. Health education should form part of the school programme, and must be associated with proper instructions of the teachers in hygiene.

As regards education of the adult, the use of the spoken and the printed word and of devices like exhibitions, cinema films and radio talks are mentioned, but the campaign to be successful should be continuous and the messages should be repeated over and over again in different form and manner.

#### 'CO-OPERATION IN THE CAMPAIGN AGAINST TUBERCULOSIS' BY DR. R. KRISHNA

Tuberculosis is a disease whose tentacles spread into various fields of human activity. The anti-tuberculosis campaign to be successful must have co-operation of all bodies concerned in the prevention and treatment of the disease.

The importance of the general practitioner in establishing early diagnosis and in connection with schemes for organized home treatment apart from a clinic is emphasized. Various forms of co-operation with the maternity and child-welfare organizations, public health departments, and school medical officers, as well as with other social agencies are given.

#### Discussion

While doubt was expressed as to the value of much of the usual type of propaganda, the discussion generally recognized that a true and well-organized propaganda was one of the essentials of the tuberculosis campaign. The facts should be placed before people, but emphasis should be on the side of hope, and not of horror. Public co-operation in the campaign could only be obtained by the right type and method of propaganda and education, beginning even in the schools.

#### 'LEGISLATION AND TUBERCULOSIS' BY DR. A. C. UKIL

The growth of sanitary law in the civilized world is traced. History of tuberculosis campaigns in the western countries shows that the first initiative has been taken by private agencies and the State came later to extend, regulate and co-ordinate action of these bodies especially with regard to finance and legislation. In no country except the United States of Soviet Russia has the State completely taken over the task of the tuberculosis campaign and in most countries a joint action has been favoured.

Tuberculosis legislation in England, especially in regard to notification of cases, provision for an anti-tuberculosis campaign, co-ordination of the administrative machinery of the component parts is mentioned in some detail. Defects in regard to notification of tuberculosis in India are detailed.

The opinion is expressed that the time has not yet come in India for any comprehensive and useful tuberculosis legislation, although it may seem urgent and important. It is suggested that in the interim period the provisions of the Municipal Acts, Rural-Health Acts, be administered with zeal and sympathy and that more powers be delegated to the medical officers of health. Legislation for action in regard to factors which indirectly help anti-tuberculosis campaigns such as rural and town planning, slum clearance and housing to prevent overcrowding and insanitary living, especially in urban and industrial areas is favoured. Spitting on the floors and walls on public roads and public vehicles should be made a punishable offence.

#### Discussion

Discussion emphasized the necessity of educating and influencing municipal and local authorities in tuberculosis matters as one of the most important parts of the campaign. Enabling legislation was in the earlier stages to be preferred to coercing legislation, as legislation should not be too much in advance of public opinion. Later, mandatory legislation should come.

## Medical News

### BRITISH MEDICAL SERVICES. WAR-TIME REORGANIZATION AND IMPROVEMENTS

BRITISH medical services, before the war, had a world-famous reputation. It is possible that war-time reorganization may be responsible for permanent improvements which will maintain and increase that reputation.

Formerly, British hospital services were of two kinds—voluntary and municipal. There were roughly 900 of the former and 1,800 of the latter.

The voluntary hospitals were started by charitable contributions, and in many cases were not allowed by the terms of their foundation to charge fees. They often specialized in some particular form of complaint, such as those associated with the eyes, with ears, nose and throat, or with the chest. In addition they were directed by leading specialists in these complaints, who were able to obtain private practice as well as prestige from such appointments.

The municipal hospitals, on the other hand, were maintained by local taxation and had full-time staffs.

The doctors were paid comparatively low salaries—£350 to £500 a year—much below what a specialist would have to earn in order to maintain his consulting rooms.

The support given to voluntary hospitals was magnificent, but for some years before the war this system had been working with difficulty. As the number of voluntary hospitals increased, so, automatically, did the number of specialists and Harley Street, the famous thoroughfare in which the majority of great specialists have their consulting rooms, gradually became overcrowded. The prospects for the specialist also decreased. Moreover, as the voluntary hospital services improved, the middle classes (who could not afford to pay a specialist) were more willing than ever to enter the public wards of the voluntary hospital where the hospital specialist worked, rather than go to a private nursing home.

This also increased considerably the voluntary hospital expenses. For these reasons it was possible that the voluntary system might soon have broken down

in any case, and that a good deal of hardship may have arisen from the resulting dislocation.

But at the outbreak of war, the British Ministry of Health took over both the municipal and the voluntary hospitals in order to provide the 300,000 beds necessary for possible air raid casualties. The Ministry is now paying the doctors (many of them specialists) as well as maintaining the voluntary hospitals. The immediate future of these institutions seems secure, and it is difficult to believe that when the war is over they will return to the old haphazard system of relying on voluntary contributions.

But State support for the voluntary hospitals is only one of the advantages which war has brought. Under the old system, the specialized hospitals were crowded into London without regard for the needs of the rest of the country. This fault has now been corrected by dividing Britain into eleven regions, each with a centre that can become the centre of a peace-time medical service.

Another advantage under the new system is that the big hospitals have only small casualty clearing stations in London, the main base hospitals being out in the country. Obviously a hospital in the country can be more spacious, more restful for the patients, and cheaper than one in town. What far-seeing doctors have been striving to attain for years, the British Ministry of Health have accomplished in a few weeks.

[We are pleased to publish this news item which was sent to us by the Deputy Principal Information Officer, Delhi, but we feel we ought to add that the hospital problem in England has not been solved overnight as satisfactorily as the writer of this note seems to suggest. There is another point of view, and there are many who think that the present temporary hospital arrangements are far from satisfactory and are not likely to be accepted even as the basis on which future medical organization in England will be built. The fact, however, that the British system of depending on honorary visiting physicians and surgeons is threatened should make those who demand the wholesale adoption of this system in India hesitate.—EDITOR, *I. M. G.*]

#### DISPUTE OVER NAME 'GLAXO'

GLAXO LABORATORIES, LIMITED vs. GLAXO SURGICAL COMPANY

In a suit filed by Glaxo Laboratories, Limited, of Greenford, the well-known manufacturers of Glaxo products, against Glaxo Surgical Company of Sialkot City, in the High Court, Bombay, the plaintiffs' case was that they had for several years imported into and

sold in India pharmaceutical and medical preparations through H. J. Foster & Co. of Bombay; that on almost all such products the name 'Glaxo' appears prominently; that one of such products, a baby food by the name of 'Glaxo', which contains the word 'Glaxo' printed in a distinctive style, has become very popular all over India; that the word 'Glaxo' on any product has come to connote to the public that it is a product of the plaintiffs; and that the word 'Glaxo' appearing as part of the name of any concern has come to connote that such concern is connected with the plaintiffs. They complained that the name of the defendants was so similar to their name as to deceive and that the defendants had by circulars and otherwise advertised and sold surgical products such as hypodermic syringes and stethoscopes under the name 'Glaxo' printed in the distinctive style in which it is used by the plaintiffs, and that such products had been purchased by certain members of the medical profession under the belief that they were the products of the plaintiffs, which they were not.

At the hearing of the suit on the 22nd December, 1939, a decree was passed granting the plaintiffs a perpetual injunction restraining the defendants, their servants and agents from carrying on business under the name of 'Glaxo Surgical Company' or under any name which contains the word 'Glaxo' or under a name which is calculated to deceive the public into believing that it is connected with or associated with the business of the plaintiffs, and from selling or from advertising for sale their products under the name 'Glaxo' or a colourable imitation thereof or in a manner likely to mislead the public into believing that they are products of the plaintiffs. The court further ordered the defendants to deliver up for destruction before the 15th January 1940, all stocks in their possession of letter paper, bills, circulars, leaflets, stationery and goods bearing the name 'Glaxo Surgical Co.' and the word 'Glaxo'.

#### THE BIRTH CONTROL RESEARCH COMMITTEE

THE total number of people who visited and sought advice at the Free Birth Control Centre conducted by the Birth Control Research Committee of Vile Parle at Dadar, during the year ending 15th December, 1939, was 2,896, out of which 1,212 were males and 1,684 were females. The office of the Birth Control Research Committee and the Birth Control Centre will be shifted from 1st of January, 1940, to Empress Mahal, Block No. 4D, Khodabad Circle, opposite the tram terminus, Dadar, Bombay 14.

## Current Topics

### Medical Treatment of Gas Casualties

(Abstracted from the *Air Raid Precautions, Handbook No. 3*, 1st edition, London, His Majesty's Stationery Office)

(Continued from page 43 of the previous number of the Gazette)

#### Need for Preventive Treatment in case of Mustard Gas Contamination

In reading what follows on the treatment of persons contaminated by mustard gas, it should be remembered that many of these may also be suffering from wounds or physical injury. Such casualties will have to be dealt with according to the particular circumstances of the case, but the treatment for contamination should follow that laid down in the later sections of this chapter so far as is compatible with the nature of the wounds. Clothing should be completely removed,

and the patient himself thoroughly cleansed in order to remove the contaminant, before the wounds are dressed.

Preventive treatment consists essentially in the speedy and complete removal of all contaminated clothing and in freeing the skin from the contaminant, whether liquid or vapour.

Exceptions to, or modifications of, this general rule may be met with, as, for example, in the case of a small localized liquid contamination of the bare hand, or after exposure to a low concentration of the vapour, when prompt local cleansing of the skin or a change of clothing respectively will suffice.

In view of the rapid penetration of the skin by mustard gas, treatment should not wait until a doctor is called, and it is part of the training advocated that all members of air raid precautions services, and as far as possible the general public, should be taught to undertake treatment for themselves. Nevertheless it is a matter of importance that it should be thoroughly understood by doctors.

Each case will have to be considered on its merits; but, whatever the type or extent of the contamination, *speed is the essence of all preventive treatment*. Delay of a minute or two in the case of liquid contamination, or of ten to fifteen minutes following exposure to the vapour, before cleansing of the skin is undertaken enhances the danger and may result in definite burns of the affected areas.

When the skin is hot as a result of exercise, and in hot or tropical countries, the results obtained by all preventive methods of decontamination of the skin are inferior to those obtained when the skin is cool and dry, and the need for prompt action is even greater.

After removal of all contaminated garments (which must not be used again until decontaminated) preventive treatment of the skin should be undertaken without delay. The choice of methods is not large, but one or more of them should be readily available at all times. The method adopted must be that which can be most promptly applied.

### Preventive Treatment for Contamination from Mustard Gas Vapour

After contamination with the vapour of mustard gas—i.e., after exposure to an atmosphere contaminated with the gas, or when the outer clothing has been sprayed, or has otherwise come in contact with the liquid form of the gas—preventive treatment should consist of a rapid removal of all clothing followed as soon as possible by a thorough washing of the whole body surface with soap and water, preferably under a shower.

Lavage of both eyes with warm water or normal saline should be carried out as soon as possible, and should be repeated every two hours. Similarly, the effects of vapour contamination of the nasopharynx may be minimized by prompt irrigations.

### Preventive Treatment for Liquid Mustard Gas Contamination

The following methods are possible:—

(a) *Bleach treatment*.—Thoroughly rub into the affected area, for a minute or so, either bleach ointment or other approved protective ointment, or aqueous bleach paste. This procedure chemically neutralizes the mustard gas.

As a first step in the prevention of burns, when the contamination is small and localized, thorough rubbing with the ointment is the method of choice. For extensive contamination by the liquid, however, a thorough inunction with aqueous bleach paste will be found more easy of application.

When the operation is completed the ointment should be wiped off, or, if the aqueous paste was used, the affected part should be flushed with water—the object being, in each case, to remove surplus bleach from a potentially injured area. Bleach will destroy free mustard gas quickly, but it will also irritate the skin if left in contact with it. Care must be taken to prevent access of bleach to the eyes.

Bleach should not be used if an erythema has already developed, as it aggravates the condition.

Actual vesication of the skin by drops from mustard gas spray may be avoided if preventive treatment be undertaken within a minute or two after contamination. Even though the delay be longer, bleach will still be the method of choice so long as liquid mustard gas is visible on the skin, as it will mitigate the severity of the resulting burn.

Bleach ointment is made by mixing equal parts, by weight, of 'supertropical' bleach and white mineral jelly, while the aqueous bleach paste consists of 'supertropical' bleach mixed to a creamy consistency with water—roughly, one part of bleach to one or two parts of water by volume. The ointment keeps well in temperate climates, while the aqueous paste retains its effectiveness for several days if it be stored in enamelled containers with well fitting lids; for tropical climates a special protective ointment is desirable.

Bleaching powder is ordinary chloride of lime, while 'supertropical' bleach is the same substance stabilized by the addition of quicklime, and fulfilling certain conditions of stability and chlorine-content.

Ordinary bleach is more irritating to the skin than the supertropical variety, but in the absence of the latter is suitable for preventive treatment when made up as an ointment with white mineral jelly, or into a paste with water, provided prolonged storage is not required.

The use of white mineral jelly is essential; yellow mineral jelly in contact with bleach may generate heat, and may even produce combustion on storage. If mixing is carried out in bulk, the employment of a mill is advocated in order to ensure a thorough and uniform consistency.

(b) *Removal of contamination by means of a solvent*. Swab the contaminated area repeatedly with petrol, kerosene, carbon tetrachloride, or other solvent of liquid mustard gas.—It is important to remember that these solvents do not destroy the gas, but merely dissolve it; hence the swabbing must be confined strictly to the contaminated area, and must be repeated.

This method is effective if carried out by skilled individuals, and solvents are within easy reach; certain precautions, however, are very necessary. Oil-skin or rubber gloves must be used if available; otherwise, the swab should be only partly immersed in the solvent, and it should be held between finger and thumb by the dry portion, or preferably in forceps, the wet portion is then applied to the contaminated skin so as to soak up the liquid contamination, care being taken that none of the solvent runs over the skin of either the subject or the operator; the contaminated swab is then discarded and the process is repeated for several minutes with fresh swabs, or as long as the characteristic odour of the gas persists on the skin. Thorough washing with soap and water, if available, will complete the treatment. The contaminated swabs must, of course, be destroyed by burning and the gloves and forceps decontaminated.

One disadvantage of this method in the hands of unskilled persons is that the solvent is apt to 'run' on the skin and cause burns on areas comparatively far removed from the original site of contamination; a further disadvantage is the liability of the operator's fingers to become contaminated in the absence of gloves. Employed with care and intelligence, however, the method is valuable in an emergency.

(c) *Thorough washing*.—Wash thoroughly the affected part with soap and water, using frequent changes of water. This process does not destroy the mustard gas, but merely removes it in the lather; the scrubbing must, therefore, be confined to the contaminated area, and the hands should be safeguarded, if possible, by suitable gloves.

If the liquid contamination be small, localized and of known situation, this is an effective method of removing it if carried out promptly. In any case, vesication of the skin is usually prevented if the treatment is not delayed beyond five minutes, though an erythema will probably result.

With a gross contamination, or when the drops of liquid mustard gas are multiple, the results of scrubbing with soap and water are unfavourable, as it is difficult to avoid spreading the contaminant in the soapy lather to surrounding areas. Under these circumstances bleach treatment is the method to adopt if available.

Should it not be possible, however, to deal with such a contamination until some time has elapsed, thorough washing should still be carried out at the first available opportunity in the hope of mitigating the degree of burning.

(d) *Special treatment for eyes*.—Apart from the skin surfaces, the only other areas to which preventive treatment can be extended are the eyes.

Contamination of the eye by liquid mustard gas presents a very serious problem. Should an eye be contaminated by the liquid, however small the drop may be, immediate preventive treatment should be



undertaken. None of the methods recommended for the skin is applicable for this purpose; simple, but rapid, removal of the contaminant by bland, unirritating methods is indicated.

This may be done by thoroughly flushing out the conjunctival sac with warm, plain water, or some bland solution, after opening the eyelids wide. This flushing should be most thorough and should be repeated hourly in the hope of mitigating the damage to the eye. If evidence of local irritation appears, a drop of liquid paraffin or castor oil should be instilled to prevent the eyelids adhering. Cocaine is contra-indicated.

### Curative Treatment for Mustard Gas Casualties

The first essential in the treatment of mustard gas casualties is the prevention of further infection from contaminated clothing; it will be necessary, therefore, to strip the patient completely and to wash the entire body surface, employing frequent changes of soap and water. The opportunity should also be taken at this stage to douche the eyes thoroughly.

The second essential is to relieve immediate symptoms.

The question of treatment is best dealt with by taking in succession the various parts affected.

#### (a) TREATMENT OF THE EYES

Although liquid contamination of the eye may produce some irritation on contact, this usually subsides and may be followed by an absence of symptoms lasting about half-an-hour. Within one hour, however, the eye is red and swollen, and the lids are half closed. It should be unnecessary to stress the futility of waiting for such signs, or for subjective symptoms to appear before undertaking systematic treatment. The risks attending liquid contamination of the eye are so grave that any history of such an accident should be sufficient to justify immediate and thorough treatment.

At this early stage treatment is limited to thorough and frequent lavage of the eye with a warm 2 per cent solution of boric acid, or normal saline solution, in the hope of mitigating the severity of the inevitable lesion.

After the onset of clinical signs, treatment is largely symptomatic, and in the earlier stages will be confined mainly to the relief of pain and to free irrigation; the latter, however, will present some difficulty owing to the intense photophobia and blepharospasm which exist, and the general cedema which pervades the tissues.

When spasm and pain are marked the application of sterilized 1 per cent atropine ointment (or perhaps an aqueous solution or lamellæ) every 12 hours will give relief, and in all cases where the cornea is affected this treatment should be persisted in. Cocaine should not be used to allay the pain, as this drug, which exerts only a transient anæsthetic action, tends to loosen the corneal epithelium and facilitate ulceration.

Free drainage of the discharge is essential, and on no account should the eye be bandaged as this will only result in damming back the secretions with disastrous results. Shades of brown paper or other light material may readily be improvised to relieve the photophobia, and a few drops of sterilized liquid paraffin may be inserted several times a day to prevent the eyelids becoming glued together and impeding free drainage.

When the discharge becomes muco-purulent the instillation of a weak (2 per cent) solution of argyrol or protargol twice daily will be found useful. This treatment is of particular importance when the cornea is grey and roughened, in order to avoid the danger of an infiltrating ulceration. Should this occur, the ulcer may be cautiously cauterized by the light application of pure carbolic acid put on with a nearly dry brush slightly moistened with the liquid. Frequent bathing and hot applications over the closed lids four times a day will assist in relieving pain.

If hypopyon supervenes and does not clear up with hot bathing, atropine and frequent cleansing of the conjunctival sac, Saemisch section is indicated.

With vapour contamination of the eye the prognosis is very much more favourable, and it is important that the patient be reassured from the outset that his eyesight will not be lost. Treatment, however, must be prompt and assiduous, as all contamination of the eye, however light, is a prolific source of invalidism.

For mild cases, where exposure to the vapour has been of a short duration, frequent lavage or warm irrigations every two hours will suffice to clear up the condition. The instillation of a few drops of liquid paraffin will prevent the tendency of the eyelids to adhere, and a quiet, darkened room or an eye-shade will materially add to the patient's comfort if any degree of photophobia be present. An astringent lotion and general tonic treatment will complete the cure.

In more severe cases, however, both pain and spasm may be marked, and the cornea may be affected. Under these conditions the treatment should be on the lines of that recommended for cases of liquid contamination, the primary indication being the prevention of corneal ulceration or the formation of adhesions.

#### (b) TREATMENT OF THE RESPIRATORY TRACT

The early rhinitis is usually overshadowed by the condition of the eyes; should there be pain and distressing discharge it may be treated with copious warm douches of sodium bicarbonate in 5 per cent solution several times daily. In the rare cases where a persistent muco-purulent discharge, associated with ulceration and occasionally with epistaxis, is long continued, an astringent lotion containing zinc sulphate with boric acid will be found helpful.

**Laryngitis.**—The laryngeal irritation is best dealt with by topical treatment such as laryngeal spraying or by the inhalation of steam from a pint of boiling water containing a teaspoonful of a mixture of menthol grs. 10 in 1 oz. tinct. benzoin. co.

**Broncho-pneumonia.**—As the majority of deaths from mustard gas in the last war were due to secondary infections of the respiratory tract, treatment should be directed from the outset towards combating bacterial invasion of the bronchi.

As a preliminary step against extraneous infection, all cases of mustard gas poisoning in which the respiratory tract is involved must be kept apart from other patients suffering from infective pulmonary disorders; they should, if possible, be segregated in special wards, and the onset of broncho-pneumonia in one of them should entail his isolation.

The routine employment of volatile antiseptics from the earliest stage will be facilitated by the adoption of a pliable, perforated mask, fashioned in the form of a Burney Yeo inhaler, containing a pad of gauze on which a few drops of the antiseptic are placed hourly. A useful formula is the following:—

Menthol	..	..	gr. 20
Chloroform	..	..	min. 60
Creosote	..	..	min. 60
Ol. Eucalypti	..	..	min. 20
Tinct. Iodi	..	..	min. 30
Sp. Vini Rect.	..	..	to one ounce

The value of menthol in mustard gassing is enhanced in those cases which require operative treatment for some concomitant wound. In these cases the laryngitis is such that, until it has been allayed by the inhalation of menthol, it may be impossible to induce anæsthesia, as the anæsthetic sets up paroxysms of coughing.

In the various stages of the broncho-pneumonia, treatment is symptomatic and follows the recognized rules of procedure, including the employment of expectorants where the muco-pus is tenacious and difficult of expulsion. It may be stated here that the prophylactic venesection advocated for phosgene cases, which is of value in the early treatment of pulmonary cedema, has no place in the treatment of mustard gas cases, though occasionally it may be indicated at a later stage to relieve the right heart of embarrassment and cyanosis induced by a diffuse broncho-pneumonia. The same may be said of oxygen therapy, which,



although essential in the pulmonary oedema caused by phosgene, is only indicated occasionally and at a late stage in mustard gas poisoning when a condition of oxygen want is established as the result of grave and widespread pulmonary damage.

### (c) TREATMENT OF THE SKIN

As in other regions of the body, septic infection is the most potent factor in delaying the satisfactory healing of skin burns. When it is remembered that mustard gas penetrates, and in so doing devitalizes, the skin, it is obvious that early preventive treatment is of paramount importance, inasmuch as it will lessen the severity of the skin burns and reduce the risk of sepsis, and that any curative treatment should have some antiseptic value.

As a preliminary to all local treatment it is essential to cleanse the skin as thoroughly as its damaged condition permits, and to clip short all hair, if any, on the affected area. It may be useful to repeat here that the application of bleach in any form to a skin which is already showing signs of damage will aggravate the ensuing burn. It must also be noted that skin surfaces damaged by mustard gas are exceedingly susceptible to trauma, and that even the continued pressure of an ill-fitting bandage may lead to an extension of the damage. As treatment will vary according to the nature and degree of the burns, it will be best to consider these in detail:—

(1) *Erythema*.—Mild cases which do not proceed beyond an erythema heal spontaneously, with possibly some desquamation and pigmentation. They may be compared to sunburns in severity and discomfort, and clear up just as readily. If the skin is unbroken a mildly antiseptic dusting powder may be applied.

(2) *Vesication*.—It is this stage that will afford a critical test of successful treatment through the elimination of secondary infection, as the devitalization of the tissues in these cases is much more profound.

Any available cleansing treatment in use in surgical practice will suffice for the undamaged skin surrounding the burn itself. In the last war extensive use was made of Eusol and of Dakin's solution for the treatment of burns, but they are too painful for continued use on raw surfaces. Picric acid and similar powerful germicides are undesirable because of the toxic symptoms that may follow their absorption, while ointments and pastes are, as a rule, contra-indicated because of their tendency to seal up discharges; for the same reasons powders are undesirable as they are apt to produce crusts which retain the discharge.

When discrete, circumscribed blisters make their appearance they should be evacuated, with an aseptic sterile needle, gentle pressure being applied, if necessary, upon the walls of the blister with a sterile swab to ensure complete evacuation; the intact epithelium should then be allowed to collapse and seal down the raw, sensitive surface underneath. This evacuation of fluid from blisters may have to be repeated owing to the continued oozing of serum from the raw area; if this procedure be delayed some hours the serum may be found to have coagulated, in which case the overlying epithelium should also be removed. The further treatment of these circumscribed vesicles consists in the application of dry dressings.

Satisfactory results have followed the use of crude cod liver oil in the treatment of comparatively small mustard gas burns after evacuation of the blister and removal of dead skin; the healing of the burns was rapid. The oil is freely applied on lint, which is then covered by a pad of cotton-wool. The dressings are changed daily; little or no irritation is caused, and the oily dressings come off easily and without pain.

When larger areas are affected, however, and when the blisters are confluent, better results will follow the use of a non-irritating antiseptic such as 'Dettol' made by adding 20 per cent by volume of 'Dettol' to a freshly prepared 5 per cent solution of tannic acid. After evacuating all blisters and removing the loose epithelium, the solution is applied directly to the raw surfaces either as a spray or, preferably, on lint, as a

coagulum appears to form more quickly on a moist dressing than when an atomiser is used. Three or four layers of the lint are soaked in the mixture and applied to the burnt area, which is then covered lightly with cotton-wool and a gauze bandage; the cotton-wool and bandage may be removed every two or three hours, but the lint is left in position and is re-soaked. The entire dressing may be removed at the end of 8 to 12 hours, by which time a firm coagulum has formed; this is then sprayed with 4 per cent tannic acid solution and dried.

A further step towards the reduction of possible infection may be taken by swabbing a large area surrounding the burn with the antiseptic, for the sepsis which sometimes occurs at the edges of the coagulum appears to originate from the surrounding skin; further, it is advisable to repeat this swabbing every four to six hours until the coagulum has separated.

After the separation of the coagulum, the general principles of wound treatment are applied to the unhealed areas which remain; stimulating lotions or scarlet red ointment will be found of use in encouraging the growth of new epithelium.

In cases where the condition is already septic, continuous baths, at body temperature, of a mildly antiseptic nature will prove both soothing and efficacious, while hot hip baths of isotonic salt solution are helpful in allaying the intense irritation of mustard gas burns of the groin and genitalia. If hot compresses or fomentations be employed, lint should be used in preference to gauze as it is less painful to remove; oiled silks should be avoided, as they keep the burns sodden and retain the discharge.

### General Treatment for Mustard Gas Casualties

Where nausea, vomiting or epigastric discomfort is present, the diet should be light and fluids may be given freely; should these not be retained, the administration of 10 to 20 grs. of sodium bicarbonate may be of assistance, and the patient should be encouraged to drink water freely. As convalescence proceeds, and in all cases of uncomplicated body burns, a full diet is required, and this should be as varied as possible. Cases showing evidence of commencing fever, which may be a prelude to broncho-pneumonia, should be suitably dieted.

Experience has shown the importance of combating functional after-effects. Functional disorders fall, in the main, into two classes. In the first, exposure to gas, often to a minimal and barely toxic concentration, may yet prove the final factor in upsetting a nervous system already breaking down as the result of physical or mental strain. In such circumstances, and especially when combined with ignorance, it may produce an 'anxiety state' similar in all respects to the neurosis so common in the last war.

The second class is a more important one, because in these cases a local, but real, organic lesion from mustard gas causes certain irritant reflexes, such as coughing or photophobia, and these sensory reflexes are perpetuated by introspection, almost in a form of conversion hysteria, long after their organic cause has been cured. Lack of appreciation of this possibility by doctors will cause much delay in discharging casualties.

Functional photophobia and aphonia are responsible for the great majority of cases. This is not surprising when it is realized that the initial trauma affects a highly organized special sense, and the fear of blindness or dumbness resulting from the injury may very well act to prolong the symptoms. Ill-advised and unnecessary treatment, however, is also a probable factor in many cases, as, for example, the continued retention of eye-shades long after the necessity for them has passed and the actual lesions have totally disappeared. There can be no doubt that the suggestive influence of wearing a shade under these conditions will prolong the functional manifestation.

Persistent aphonia, often accompanied by a useless, harsh cough is another striking evidence of auto-suggestion arising from the initial laryngeal irritation.

The characteristic cough is either dry, or accompanied by watery sputum mainly of salivary origin; it is usually much worse at night, and is of a ringing, harsh quality. If the doctor realizes the nature of the condition and gives the patient confidence in his early recovery, this functional aphonia yields very rapidly to treatment by suggestion and breathing exercises.

## Weil's Disease in the North-East of Scotland An Account of 104 Cases

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DURING the past few years increasing attention has been paid to the clinical, bacteriological, and epidemiological aspects of Weil's disease, with the result that it has been found to be much more prevalent and more widely distributed than was originally anticipated.

**Occupational incidence.**—Of 104 cases reported in this paper ninety-eight occurred in fish workers (filleters, curers, porters, and carters). The remaining six were in farm workers (two), labourers constructing sewers (two), and an engineer in a rag factory, and one arose from harbour immersion. One case occurred in Aberdeenshire and three in Kincardineshire, the remainder arising in the city of Aberdeen. A study of the streets in which the one hundred patients were employed showed that ninety-seven worked in a small area adjacent to the harbour and the fish market.

An investigation into the distribution of the ninety-seven cases in relation to the numerous fish-curing yards in Aberdeen showed that infection had been contracted in no fewer than fifty-three different establishments. It is worth noting that one firm with a large number of employees has never had a case of Weil's disease during the past five years. Accordingly we investigated the working conditions, and found that the type of work undertaken was almost entirely connected with the salt fish trade, in contrast to all the other establishments where Weil's disease has occurred, which specialize in the fresh fish trade.

An analysis of the monthly distribution of cases in each of the five years suggests that Weil's disease occurs least often in February and March (a total of four cases in five years) and most often in August and September (thirty-one cases in five years).

**Age and sex incidence.**—There were fifty cases in males and fifty-four in females. The total number of males employed in the industry is 786 and the number of females 1,277. Nearly half the cases occurred before the age of 20 and that four-fifths of these patients were females. This finding is related to the working conditions of the fish trade, in which young girls between the ages of 15 and 20 carry out the procedures of cleaning, gutting, and filleting fish. Between 80 and 90 per cent of the workers below the age of 20 are females, whereas after the age of 30 the majority of the employees are males engaged as foremen, porters, carters, etc.

**Mortality rates.**—The figure of 5.7 per cent is a little over one-half of that obtaining in Holland. We ascribe the low death rate to the high incidence of healthy young girls in the trade. There were no deaths among the fifty-four females. The effect of advancing years in increasing the dangers of the disease is well brought out by the four deaths among the nine patients over 50 years of age. The same tendency is noted in regard to morbidity. In general, middle-aged and elderly patients were more seriously ill than young ones. The liver in such patients seems to be peculiarly susceptible to the toxæmia of Weil's disease, and if in addition there is a history of an alcoholic tendency the prognosis becomes correspondingly more serious. At least two of our fatal cases gave a history suggestive of having partaken of excessive spirits over a long period.

## CLINICAL MANIFESTATIONS

### General

The course of the disease may be divided into three stages. The first or febrile stage lasts approximately one week, and during this time septicæmia occurs, antibodies are not detectable in the blood, and spirochaetes are not found in the urine. The patient is suddenly taken ill and complains chiefly of headache, vomiting, and severe muscular pains all over the body. In severe cases there is marked prostration, and the temperature rapidly rises to 102–104°F. The table gives the percentage incidence of the various symptoms and signs in the 104 cases. Since jaundice rarely appears before the fifth day of the illness a diagnosis of influenza is usually made. The presence of a marked conjunctivitis (pink-eye) and the evidence of a toxic nephritis (albumin, cells, and casts) may be helpful in suggesting the correct diagnosis, particularly if the patient is employed in an occupation in which the hazard of leptospiral jaundice is high.

Percentage incidence of clinical manifestations  
in 104 cases

Symptoms	Present in	Percentage
Sudden onset .. ..	104	100
Initial chill .. ..	71	68
Fever .. ..	103	99
Headache .. ..	91	87
Muscular pains .. ..	103	99
Prostration .. ..	46	44
Vomiting .. ..	84	80
Cough .. ..	18	17
Pharyngitis .. ..	34	32
Conjunctivitis .. ..	83	79
Icterus .. ..	68	65
Hæmorrhages: mild ..	61	58
severe ..	19	18
Enlarged liver .. ..	28	26
Palpable spleen .. ..	1	0.9
Adenopathy .. ..	13	12
Meningitis .. ..	10	9

The second or toxic stage is characterized by the absence of spirochaetes and the development of antibodies in the blood and the excretion of organisms in the urine. If jaundice has not appeared by the beginning of the second week the case may be considered to be mild; the symptoms then rapidly abate. In moderately severe cases which are going to do well the fever abates and the clinical condition improves; but the jaundice continues for another week or two, and the signs of a toxic nephritis are present for at least a month. In cases doing badly the jaundice becomes intense, the urinary output falls, the blood urea rises rapidly, purpura into the skin and from the mucous membranes occurs, and a falling blood pressure and steadily mounting pulse indicate the gravity of the situation.

In the third stage there is further development of antibodies in the blood. The distressing symptoms gradually subside, but convalescence is greatly prolonged in those who have been seriously ill. An interesting second rise in temperature occurs during the third week of the illness in approximately half the cases.

**Meningitis.**—In ten cases the symptoms and signs were strongly suggestive of meningitis. The clinical diagnosis was confirmed in each case by examination of the cerebrospinal fluid.

**Blood examination.**—Red and white cell counts and hæmoglobin estimations were carried out in a series of cases. The leucocyte count varied, according to the severity of the disease and the individual's response to the infection, from 10,000 to 30,000 leucocytes per c.mm. of blood. The increase was essentially due to an excess

of neutrophil polymorphonuclear leucocytes, and a typical shift to the left was noted. The red cell count and hæmoglobin were consistently reduced in all cases in which toxæmia was severe, and particularly if purpura was a prominent symptom. In such cases an erythrocyte count of 2,500,000 to 3,500,000 with a hæmoglobin concentration of 40 to 60 per cent was not uncommon. In one case with severe purpura the erythrocytes fell to 1,400,000 and the hæmoglobin to 26 per cent, and a transfusion of blood had to be given.

**Biochemical estimations.**—The icteric index was estimated in eighty-three cases. In 80 per cent a figure of 10 units or higher was found. Figures for the blood urea are available in eighty-two cases. In 60 per cent a figure of 40 mg. per 100 c.cm. or over was found. Of the six fatal cases one patient died with anuria shortly after admission to hospital, and no figures are available for either the blood urea or the icteric index. Four died with the blood urea greatly increased—namely, 161, 250, 300, and 397 mg. per 100 c.cm. In the sixth case the blood urea was only 89 mg. per 100 c.cm., but this estimation was made on a sample of blood removed on the fourth day of the illness. The patient died at home on the eighth day after the onset, without being admitted to hospital. It is obvious, therefore, that a high blood urea is a sign of serious prognostic importance. Nevertheless it must be remembered that recovery can occur despite a greatly increased blood urea. Thus we have had seven patients recover whose blood urea was respectively 128, 128, 143, 152, 161, 202, and 300 mg. per 100 c.cm. With regard to the icteric index in the fatal cases, the figures were 60, 63, 67, 89, and 150. In contrast, in patients who have recovered we have obtained figures of 100, 166, and 187. In the six fatal cases death occurred between the eighth and tenth days of the illness, by which time the maximum degree of jaundice may not have developed.

#### TREATMENT

(a) *Symptomatic.*—Treatment on the general lines suitable for any severe febrile disease is required. This includes rest, good nursing, tepid sponging, and the use of diaphoretic, analgesic, and hypnotic drugs. A simple alkaline mixture containing potassium citrate, sodium bicarbonate, and liq. ammon. acetatis is worthy of trial for combating the gastritis and facilitating the urinary excretion. The diet should be low in fats and protein and rich in carbohydrate, since hepatic and renal damage is present. Plenty of fluids and fruit juice, sweetened with glucose, should be given frequently. Iron in full doses will be required to correct the hypochromic anæmia which so often develops.

(b) *Specific.*—Ample evidence has been accumulated in Holland and elsewhere in regard to the value of anti-leptospiral serum. A reduction both in the mortality of the disease and in the severity of the toxæmia has been shown to result, particularly if the serum is given early—that is, within the first four days. After the seventh day, when the septicæmic stage is over, the beneficial effects are much less marked. The amount of serum advocated is 10 to 20 c.cm., given intramuscularly or intravenously, the dose to be repeated in four to six hours as required.

#### LABORATORY FINDINGS IN WEIL'S DISEASE

The final diagnosis of Weil's disease is largely dependent on the recovery of leptospiræ from the patient or on the demonstration of immune bodies in the serum when convalescence is being established. In this investigation culture of the blood for leptospiræ has not been extensively employed. When specimens of clotted blood were sent for examination the serum was removed for serologic and biochemical examination, and the clot was then injected intraperitoneally into two young guinea-pigs. Up to the fourth day after the onset of illness the leptospira could be recovered from all cases. After that day the chance of recovering the organism rapidly decreased until on the seventh

and eighth days it was found in the blood of exceptional cases only. These results are in accord with those reported by Japanese workers.

In no case was a positive serum reaction obtained before the third day after the onset. Thereafter the immune bodies rapidly increased in the serum until on the fifth day 50 per cent, and by the ninth day 100 per cent, of cases had given a positive reaction. Furthermore, the actual titre of the serum also increased from 1 in 10 in the early stages to 1 in 10,000 or 1 in 30,000 or more by the tenth day. In only three cases were leptospiræ isolated from the blood at a time when immune bodies could be demonstrated simultaneously in the serum. In case 37 the blood taken on the sixth day showed the presence of leptospiræ and a positive serum reaction of 1 in 30; in case 72 the specimen was collected on the fourth day and gave a positive result on guinea-pig inoculation and an agglutination reaction of 1 in 30; and finally in case 81 the blood showed leptospiræ on the seventh day and a weak serum reaction of 1 in 10.

The leptospira can also be recovered from the urine, but it is essential that the specimen must be inoculated into guinea-pigs as soon as possible after being passed. Two hundred and eleven specimens of urine from eighty-eight cases of proved Weil's disease were tested by this method. In no instance has it been possible to recover the leptospira from specimens collected within the first seven days of the disease. In the period eight to fourteen days after the onset 19.3 per cent of samples were positive, in the period fifteen to twenty-one days 21.5 per cent, and in the period twenty-two to twenty-eight days 9.5 per cent. Thereafter the results were negative. It would appear, therefore, that at no time during the course of the illness can virulent leptospiræ be recovered with certainty from the urine.

Agglutinins may also be demonstrated for *L. icterohæmorrhagica* in the urine of patients convalescing from the disease. This is probably due to the fact that albuminuria is a constant feature of the disease, and the immune bodies are excreted in a dilute form attached to the euglobulin.

#### The Clinical Application of Testosterone

By WALTER M. KEARNS, M.D.

(Abstracted from the *Journal of the American Medical Association*, 3rd June, 1939, p. 2255)

UNTIL two years ago the results in male hormonal substitution were unsatisfactory. It is true that some temporary relief had been recorded at San Quentin prison after Stanley's injection of testicular mush into the musculature of the anterior abdominal wall, but the procedure was never widely accepted. Nor was the isolation of testosterone from the bull's testicle of any great clinical help, since there is little storage of hormone in the tissue and only minute amounts are extractable. The yield is so small that it would require the rendering of 100 bull testicles for the daily maintenance of one castrate. Not until the recent commercial production of testosterone has an effective method been available.

Since the isolation and identification of testosterone and the perfection of a method of synthesis by degradation of sterols, the hormone has been placed on the market by several drug houses. Some esters of testosterone have been proved to be more potent and more prolonged in their effect than the free hormone. Testosterone propionate is the combination offered by the manufacturers.

The advent of these potent preparations has resulted in exaggerated claims and theories which expand beyond the limits of reasonable speculation. The medical literature is already being cluttered with premature reports demonstrating a lack of knowledge that may result in confusion on the part of the physician attempting to gain an understanding of a most complicated and profound problem.

## INDICATIONS

Caution in the choice of patients must be exercised, as the possibility of overstimulation and glandular imbalance must be kept in mind. Testosterone must not be injected indiscriminately into every knave who aspires to emulate the sex behaviour of the cock or the squirrel. Because of the possibility of the later atrophy of the testicles, long periods of treatment of adolescent boys and young men must be avoided unless clinical evidence of hypogonadism and low urinary output of the androgens has been demonstrated.

## CASTRATES

Six castrates were recalled from my past practice and that of two other urologists, Dr. Warren Leaper and Dr. James King. These patients had previously made the rounds of several physicians and received the usual futile ministrations with orally administered and injected preparations, ending in despair. They were broken men—nervous, apprehensive, depressed, unable to concentrate and devoid of libido, with pale sawn thin wrinkled skin—bearing their crosses tenaciously but at best barely able to hold part-time positions. True to form, these patients had had definite shrinkage in the size of their prostate glands, in some instances to such a degree that the gland was indiscernible by digital rectal examination.

Basal metabolism tests, tests for blood cholesterol, Aschheim-Zondek tests with assay of the urine for gonadotropic substance and sugar-tolerance tests were repeated periodically. Originally these patients deviated in varying degrees from the normal, with a lowered basal metabolic rate, increased dextrose tolerance and a lowered blood cholesterol content. The Aschheim-Zondek test has not been positive in a single instance. A sufficient number of recent tests to indicate any decisive changes have not yet been completed.

The most sensitive clinical indicators of testicular function are the seminal vesicles and the prostate gland. Carl R. Moore, Callow and Deanesly and McCullagh have called attention to the prompt atrophy of the prostate after castration. Experimentally, in castrated male animals the administration of androgenic agents elicits a prompt response in the increase in size of the atrophic prostate and seminal vesicles.

The injection of testosterone propionate produced a change in the patients as definite and pleasing as anything in my experience. Ten mg. administered twice weekly has completely rehabilitated them. With two, injections of 5 mg. twice weekly were sufficient. Increased strength and endurance, a desire to expand their work, the appearance of libido, erections, ejaculations, ability to copulate and an increase in the growth of the beard have all been observed in their return to normality. After from three to six weeks the prostate gland regenerates perceptibly, and it approaches the normal size in from six to eight months. One very religious patient, working as an orderly in a local hospital, threatened to discontinue treatment because of the appearance of annoying erections, and he would have deserted had it not been for the concomitant appearance of well-being and ability to work without extreme exhaustion. Foss reported that a castrate while receiving 140 mg. of testosterone in a week acquired priapism which was unrelieved by intercourse but abated several days after the dose had been diminished.

## TESTOSTERONE IN OINTMENT

About six months ago, on the suggestion of Dr. Carl R. Moore of the University of Chicago, testosterone as an inunction was employed with castrates. Moore has more recently reported on the potency of androgenic substance applied to the skin of animals.

Three of the castrated patients and two patients with cryptorchidism who were given testosterone ointment (each centimetre containing 2 mg. of free testosterone) have reported excellent results, at least equal to the effect obtained with injections. With the application of 2 c.c. each day the dose applied to the skin was

somewhat more than the injected amount. The total average weekly dose administered to the castrates was 20 mg. by injection and 28 mg. by inunction. Patients are directed to rub the ointment vigorously for twenty minutes into a hairless area of skin, preferably on the anterior abdominal wall. The application is made each day at bedtime.

Corroborating the good clinical outcome, proof of the absorption of the substance by the human skin was obtained through the demonstration of increased androgenic activity in the urine.

The potency of many drugs administered through the skin by inunction is well known to the physician. Through the ages the treatment of syphilis rested mainly on the mercurial inunction because of its proved, prompt and prolonged therapeutic action. As evidence of absorption of the mercurial through the intact skin, toxic gingival, intestinal and renal manifestations frequently developed when proper reserve was not exercised in its administration.

Macht has recently reported the result of a long and careful study on the absorption of drugs and poisons through the skin and mucous membranes. He commented on the sound rationale underlying many of the older therapeutic procedures employing inunction, pointing out the benefits and dangers as well.

The problem in substitution therapy with testosterone is to arrange the administration so as to imitate the steady continuous activity of the normal glands and avoid alternation of deficiency and wasteful excess of the hormone. In an ointment the hormone is slowly and continuously available to the body. It is possible that this method of administration of androgens may have widespread acceptance. At any rate, for patients who have difficulty in reaching the physician it offers an effective form of treatment.

## POSTPUBERAL CRYPTORCHIDISM

Two patients with postpuberal cryptorchidism, 23 and 32 years of age, have been treated. In both there was retarded development of the secondary male characteristics associated with atrophy of the testicles. Each patient had the appearance of a boy of 16 years, with small face, slender build, high pitched voice and no hair on the face or in the axillæ, with typical eunuchoid bodily form, with full hips and girdle distribution of fat, and with arm span greater than body height. The patient of 32 had a small amount of pubic hair. The penis was less than 2 inches in length and of very small calibre. After one year of treatment with antuitrin-S no change was observed. The patient married during this course of treatment and his efforts at intercourse were unsatisfactory. Eight months ago treatment with testosterone propionate was instituted in injections of 25 mg. twice weekly. The penis enlarged remarkably and in six months had more than doubled its size. Intercourse with well-defined orgasm is now being carried out three times weekly in a gratifying manner. The other patient, 23 years of age, has experienced a similar good result. In both patients the prostate gland has grown appreciably and axillary hair and a small amount of hair on the upper lip have appeared. The experience of Riches and more recently that of Vest and Howard demonstrates the need of larger maintenance doses for this type of patients, approximately double the dose used for castrates. Kenyon administered 25 mg. of testosterone propionate intramuscularly from five to seven times weekly for from twenty-eight to ninety-five days to four eunuchoids. Thereafter three of them received from 10 to 25 mg. from three to seven times weekly, with interruptions for 152, 108 and 160 days respectively. In all instances there were an early increase in the frequency of erections and a marked increase in the size of the prostate as early as the twelfth day. The penis elongated from 1 to 2 cm. in all but one case. Changes in the hair of the face, pubis and thighs and deepening of the voice occurred promptly with the large dose used. Moreover, Kenyon observed nitrogen and sodium retention and a slight increase in the body-weight.



Twenty-five mg. twice weekly proved in our cases to be the minimal dose for maintenance of well-being and continuance of gradual improvement.

A larger dose of ointment is also required for eunuchoids. Four c.c. of ointment (2 mg. per cubic centimeter) is applied daily. The total weekly dose reaches approximately 56 mg. of testosterone, which compares with the injected dose of 50 mg. a week. While the response to either method of administration occurs less promptly than in the castrate, the effect is no less definite. In fact the objective sign of penile growth offers a definite indicator of the effect. A reduction of dose results in a less satisfactory clinical course.

In this type of patient, as in the castrate, there is an unquestionable indication for endocrine therapy, because unmistakable deficiency is recognizable clinically and the reassuring response to treatment is readily observed.

In these two groups the effect of testosterone may be truly called rejuvenation. The physician may now humanely select and treat with testosterone these morbid semi-invalids with as much precision as he would use in treating with insulin patients with advanced diabetes. Testosterone may not contain all the components of testicular secretion, but it does control dramatically some processes associated with its deficiency.

#### SUMMARY

1. In castrated patients and in those with hypogonadism due to cryptorchidism the administration of testosterone brings about an effective substitution.

2. Beneficial results have been obtained through the intramuscular injection of testosterone propionate and equally good results through the inunction method with free testosterone in a greaseless base.

## Reviews

**THE ESSENTIALS OF MEDICAL TREATMENT.**—By David Murray Lyon, M.D., D.Sc., F.R.C.P.Ed. 1939. Oliver and Boyd, Limited, Edinburgh (Tweeddale Court). Pp. xx plus 448. Price, 15s.

THE writer of a book on medical treatment always considers it necessary to apologize for his choice of subject, and he invariably gives as his reason for writing the book that treatment is a subject which is very badly neglected. This excuse has now worn very thin, for the reviewer has at least half a dozen books on medical treatment all published within the last two years, and the 'therapeutic nihilism' of the last century is now deeply buried under a formidable pile of volumes, good, bad, and indifferent. However, Dr. Murray Lyon's book is a good one and did not require any explanation or excuse. It has that essential quality, readability, and, though the text is not relieved by many illustrations, it has not been made unnecessarily heavy with tables and classifications.

The book is written very much from the practitioner's point of view, though from his remarks in the preface the author seems to have the needs of the undergraduate student primarily in his mind. There is nothing contradictory here, for the undergraduate student of to-day is the practitioner of to-morrow; we do not believe that this book will help the former to get through his examinations, but we are certain that it will help him to treat his patients when he is let loose in the world of general practice.

The first chapter is on febrile diseases, and begins with a description of the treatment of fever *per se*. Other subjects discussed are tonsillitis, rheumatic fever, typhoid, malaria, and septicæmia. The author has taken literally the dictum that cholera is a febrile disease and has included it in this chapter. Successive chapters are on diseases of the various systems, on metabolic and endocrine disorders, on allergic diseases, and on diseases of the blood.

The author would have been wiser to have kept to his own personal experience and omitted such subjects as cholera, his treatment of which bears the stamp of pure transcription and is pretty poor at that; the emphasis laid on potassium permanganate betrays the source. 'For the initial diarrhoea a dose of calomel may be given or some castor oil with laudanum'; we don't understand, or agree. 'Encmata of 2 per cent tannic acid have been tried at a later stage without much result'; then why mention it!

It is much easier to criticize than to praise, and we hope that these few criticisms will be fully discounted when we conclude by saying that this is a most valuable book which we can very strongly recommend to the practitioner and to the senior undergraduate student.

**SAVILL'S SYSTEM OF CLINICAL MEDICINE: DEALING WITH THE DIAGNOSIS, PROGNOSIS, AND TREATMENT OF DISEASE FOR STUDENTS AND PRACTITIONERS.**—Edited by Agnes Savill, M.D., and E. C. Warner, M.D., F.R.C.P. Eleventh Edition. 1939. Edward Arnold and Company, London. Pp. xxviii plus 1141. Illustrated. Price, 28s.

THIS book needs no introduction as its reputation is already established. The eleventh edition has been brought up to date, but is otherwise on the same lines as its predecessors.

The reader is presented with an essentially clinical description of medicine which is very complete. Each chapter is divided into three parts. The first part describes the symptoms which may occur as a result of disease in an organ or area of the body. The second discusses the physical signs and the third part gives a classification of the various diseases affecting that region.

Nineteen contributors, each a specialist in some branch of medicine, have revised the various sections of the book. In the face of such authority one hesitates to criticise. The chapters on case-taking and the external appearance of diseases contain much of interest which is unobtainable in the average textbook. Tropical anæmias have been rather briefly dealt with. The book is suitable for students and practitioners in India and should be especially useful when read in conjunction with clinical instruction.

The volume is handsomely bound, and the coloured plates add greatly to its success.

J. G.

**NUTRITION AND DIET IN HEALTH AND DISEASE.**—By James S. Mc Lester, M.D. Third Edition. 1939. W. B. Saunders Company, Philadelphia and London. Pp. 838. Price, 40s.

THIS book was first published in 1927 and already has an established reputation, both in the United States and elsewhere. The author is a professor in a University in the southern states of North America where conditions regarding nutrition of the masses are more comparable to those in India, than they are in the northern states of America or in England and many European countries.

The scope of the book is a wide one. There are two major divisions of the subject-matter—nutrition in health and nutrition in disease; the first chapters are on the physiology of digestion and assimilation of food. The remainder of this section 'The need for food and its utilization' is made up of chapters on

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more detailed consideration of protein, the vitamins, the minerals, and other nutritional factors in dietary.

The next section deals with food products, milk and milk products, meat, cereals, fruits, etc. The third section is on diet in health from infancy to old age and during special physiological states, such as pregnancy.

The second half of the book, nutrition in disease, starts with a very important chapter on deficiency diseases. Then follow a number of chapters on diet in different diseases; there are separate chapters on important metabolic diseases such as diabetes and gout, but others are grouped, e.g., diseases of the kidneys and urinary tracts, of the digestive organs, of the blood, of the skin, etc., nervous disease, endocrine disorders and febrile diseases. All these chapters make valuable reading for practitioners and specialists.

Finally, there is an appendix in which there are numerous useful tables.

Many American writers, although they may display a profusion of 'citations' from the literature, have an irritating way of ignoring the observations of workers in other countries. Even if one admits that the best work on nutrition is done in America, this trait shakes the confidence of the reader and detracts from the value of such writings. For example, to quote American work on stone in the kidney and vitamin-A deficiency from 1935 onwards and to make no reference to McCarrison's earlier work, or to ignore Nicholls' observations on phrynoderma seem inexcusable. Further, this isolationism occasionally leads them into trouble and is responsible for the suggestion that epidemic dropsy is identical with beri-beri, the principal symptoms of the former disease being explained away as possibly due to malaria or some other associated deficiency.

However, the book is a standard work on nutrition and will be very useful to the practitioner, the sanitarian and the research worker.

**ANTENATAL AND POSTNATAL CARE.**—By F. J. Browne, M.D. (Aberd.), D.Sc., F.R.C.S. (Edin.), F.R.C.O.G. Third Edition. 1939. J. and A. Churchill Limited, London. Pp. xviii plus 622. Illustrated. Price, 21s.

ALTHOUGH antenatal care is not a panacea for all obstetric evils and although statistics do not show the beneficial results which might be expected from almost universal (in certain countries) antenatal supervision, nevertheless the subject is one of great importance.

Professor Browne points out that the disappointing results obtained from antenatal work are often due to insufficient thoroughness and knowledge on the part of the medical attendant.

It behoves all obstetric practitioners to study this subject, especially so in this country with its high maternal and fetal mortality. Improvement in this direction must lie with general practitioners, at any rate outside the very large towns. Such practitioners, lacking as they so often are in obstetric and antenatal training, will find in Professor Browne's book a splendid reference work in this branch of their profession.

Dealing as it does with the whole aspect of antenatal difficulties and dangers in a thorough and up-to-date manner, the third edition of this excellent book is of real value to obstetricians. Interesting and somewhat unusual chapters are those on heredity and on the influence of emotions upon pregnancy and parturition.

The author deals fully with the usual diseases, such as toxæmias, pyelitis, tuberculosis, heart disease, the anæmias, venereal disease and tumours, as well as malpresentations, and more uncommon conditions, e.g., chorea, neuritis, skin diseases, and appendicitis. Abortion, moles, ante-partum hæmorrhages, retroversion and contracted pelvis are described fully.

There is one chapter devoted to the uses of radiology in obstetrics, whilst post-partum conditions (or rather sequelæ which follow the puerperium such as prolapse) are catered for in the last chapter in which are also included some useful postnatal physical exercises.

Finally there are several appendices setting forth forms for antenatal or postnatal records, the medical induction of labour, hints to expectant mothers, diets, hints on conduct of clinics and figures referring to results of treatment of placenta prævia.

Altogether this is a book to be strongly recommended to practitioners and one which will repay careful study.

K. S. F.

**COMMON SKIN DISEASES.**—By A. C. Roxburgh, M.A., M.D., B.Ch. (Cantab.), F.R.C.P. (Lond.). Fifth Edition. 1939. H. K. Lewis and Company, Limited, London. Pp. xxxi plus 416, with 8 coloured plates and 179 text-illustrations. Price, 15s.

THIS invaluable textbook on skin disease has become a biennial publication, and its popularity is such that even this does not meet fully the demands for the book, for the last edition had to be reprinted within a year. Despite this short interval since the last edition, considerable additions and changes have been made; illustrations have been replaced by better ones, and fourteen new ones have been added. Other changes have been the introduction of  $r$  units for  $x$ -ray dosage, but the older, less accurate, method of giving fractions of a pastille dose is retained as well.

The new chapter on the avitaminoses is perhaps a little too short. Frank avitaminosis is uncommon in England, with the exception of avitaminosis-D which does not give rise to any skin lesions as far as one knows, and the effect of minor degrees of hypovitaminosis is largely a matter of conjecture. This is not however the case in the east and the effects of specific malnutrition are much more apparent in practice in India, so that a little elaboration of this section would be welcome in this country. On the other hand, we think that the author is well advised not to add seriously to the size of his book by introducing purely tropical skin infections.

There is little new to be said about this concisely and clearly written and very well-illustrated book, which is in our opinion little short of the ideal book for the general practitioner; with the minor proviso indicated above, this remark applies with equal force in this country.

**SURGICAL DIAGNOSIS.**—By Stephen Power, M.S. (Lond.), F.R.C.S. (Eng.). 1939. John Wright and Sons, Limited, Bristol. Pp. 228, with 51 illustrations and 15 plates. Price, 12s. 6d.

SURGICAL diagnosis is not a new idea, but we do not know of any other short and concise book which deals with this subject exclusively and completely. Such a book will therefore find a definite place in students' and practitioners' libraries, provided of course that it is up to standard. We have no hesitation in saying that this book meets this requirement.

The chapter headings follow very much the usual lines of surgical textbooks; the first three are on bones, joints, and fractures and dislocations; then they become regional, the hand, the foot, etc.; and finally symptomatic; e.g., abdominal pain in children and hæmaturia.

The text is kept strictly to diagnosis. In each chapter, after a few introductory remarks on general considerations and methods of examination, the conditions that are likely to be encountered are taken up one by one and dealt with concisely; there is seldom more than a single page devoted to any subject and more often less. The headings of the paragraphs are clear and relevant; this makes the book very valuable for quick reference. There are many text-figures and plates; these all help to make the subject clear and easy to understand, especially as the illustrations have the merit of showing exactly what they are meant to show.

It is a book that we can very strongly recommend to the house-surgeon; he will find it an invaluable book of reference, both now and later when he is in practice.

**MANUAL OF UROLOGY.**—By R. M. Le Comte, M.D., F.A.C.S. Second Edition. 1939. The Williams and Wilkins Company, Baltimore. (Baillière, Tindall and Cox, London.) Pp. v plus 295, with 55 illustrations. Price, 18s.

This book was originally intended to provide a simple introduction to urology for the beginner. The second edition presents many useful new features which widen its scope. The book has been entirely revised and made up-to-date with additions on the neuromuscular physiology and pathology of the bladder. There is also a new chapter on impotence and sterility which will be found useful by the general practitioner.

The printing, get-up and illustrations are all good. There is an excellent bibliography, which will be of use to the more advanced student. There is little doubt that the new edition will meet with a ready reception.

P. N. R.

**A TEXTBOOK OF GENERAL BACTERIOLOGY.**—By E. O. Jordan, Ph.D. Twelfth Edition. 1938. W. B. Saunders Company, Philadelphia and London. Pp. 808, with 197 illustrations. Price, 25s.

The science of bacteriology has made very rapid progress within the last decade, so much so that it is no longer confined within the limited field of study in the medical curriculum. The systematic study of bacteriology is now a separate subject by itself, a counterpart of botany and biology, and it is for this reason that practical work in a laboratory is just as important as the progressive theoretical knowledge.

In the present volume, Professor Jordan has combined the most up-to-date conceptions in bacteriology with useful practical hints and directions for an efficient working of the laboratory. The entire book of 44 chapters offers very pleasant reading and some of the more difficult aspects of bacterial variation and antigenic relationship have been dealt with in a very comprehensive and lucid way. The classification of the Bacterium into three main types, namely, *Bacterium*, *Salmonella* and *Eberthella* stabilizes many controversial and sometimes needlessly confusing sub-groups. The chapter on virus diseases includes lymphocytic choriomeningitis and recent work on virus proteins. The last five chapters are devoted to industrial and agricultural bacteriology, namely, the bacteriology of milk and milk products, bacteria and the nitrogen cycle, bacteria in the industries, the bacteria of air, soil, and water, and the bacterial diseases of plants. An exhaustive bibliography is appended as footnotes to the text.

The book is an invaluable addendum to any bacteriologist's library.

K. P. B.

**BACTERIOLOGY FOR MEDICAL STUDENTS AND PRACTITIONERS.**—By A. D. Gardner, D.M., F.R.C.S. Second Edition. 1938. Oxford University Press, London, Humphrey Milford. Pp. 274. Illustrated. Price, 6s. Obtainable from Oxford University Press, Bombay and Calcutta

This little volume of only 266 pages can verily be called bacteriology in a tabloid form and both students and busy practitioners will find in it all the most up-to-date and essential information on the subject condensed into a very small compass. The book is something more than 'notes on bacteriology', but less exhaustive than a textbook and it is this happy mean which is so useful for students generally and examinees in particular. The practical portion is completely left out and so is the Kauffmann-White scheme of antigenic structure of the *Salmonellas*, much to the relief of the beginners in bacteriology. For the sake of clarity ultra-microscopic agents, viruses, bacteriophage and border-line organisms have all been dealt with in one chapter. The reading and pen-and-ink sketch diagrams constitute a new departure in the style of getting up a scientific book and Professor Gardner is to be warmly congratulated on this small but extremely serviceable book.

K. P. B.

**ELECTRIC EXCITATION OF NERVE.**—By Bernhard Katz, M.D. (Leipzig), Ph.D. (Lond.). 1939. Oxford University Press, London, Humphrey Milford. Pp. ix and 151, fig. 31. Price, 10s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

In this monograph, Dr. Bernhard Katz of Leipzig, Germany, now a Beit Memorial Research Fellow working in the laboratories of Professor A. V. Hill, F.R.S., in London, has presented an excellent and readable review of the present status of our knowledge of the electrical phenomena in nerves and the problems of nerve excitation. The review, as the author has stated in the preface, was originally drawn up in response to an invitation from the editors of the '*Ergebnisse der Physiologie*' but could not be published there as the manuscript was refused on 'racial' grounds by the prospective publisher in Berlin.

The Oxford University Press has done a great service to all those who are interested in neurophysiology and electrophysiology by publishing the review of Dr. Katz. In such a highly technical field as electrophysiology, the writing of a clear but concise review of recent developments is no mean achievement and Dr. Katz has certainly handled the subject-matter with the tact and judgment of a sound teacher and investigator.

The book is divided into five main chapters. Starting off with some of the fundamental observations regarding the stimulating efficacy of electric currents, the author has discussed all the recent experimental work, with figures and diagrams wherever needed, of the events which follow the application of an electric stimulus to a nerve, the temporal and spatial progress of the events which lead to excitation and its continuous self-propagation along the nerve. The theoretical interpretations and deductions of many experimental data have also been included. In the concluding section, the author sums up the conflicting arguments by saying that 'an essential part in these events (nerve stimulation) is the flow of electric current normal to a cylindrical electrically-polarized membrane, and the removal of its resting charge'. It seems, and the author also agrees, that there are still considerable gaps in our knowledge of the true physico-chemical nature of the 'excitation' phenomenon in peripheral nerves, although, adequate explanations appear to have been offered for the strength-duration curves and a variety of related experiments in terms of the two time-constants of 'excitation' and 'accommodation'. Further work in the physico-chemical field has been recommended by the author for the elucidation of the complex changes that precede the propagation of an impulse.

This book is well got-up and has a rich bibliography which should be useful to other workers in the field.

B. M.

**ANATOMY OF THE NERVOUS SYSTEM: FROM THE STANDPOINT OF DEVELOPMENT AND FUNCTION.**—By S. W. Ranson, M.D., Ph.D. Sixth Edition. 1939. W. B. Saunders Company, Limited, Philadelphia and London. Pp. 507, with 382 illustrations, some of them in colours. Price, 27s. 6d.

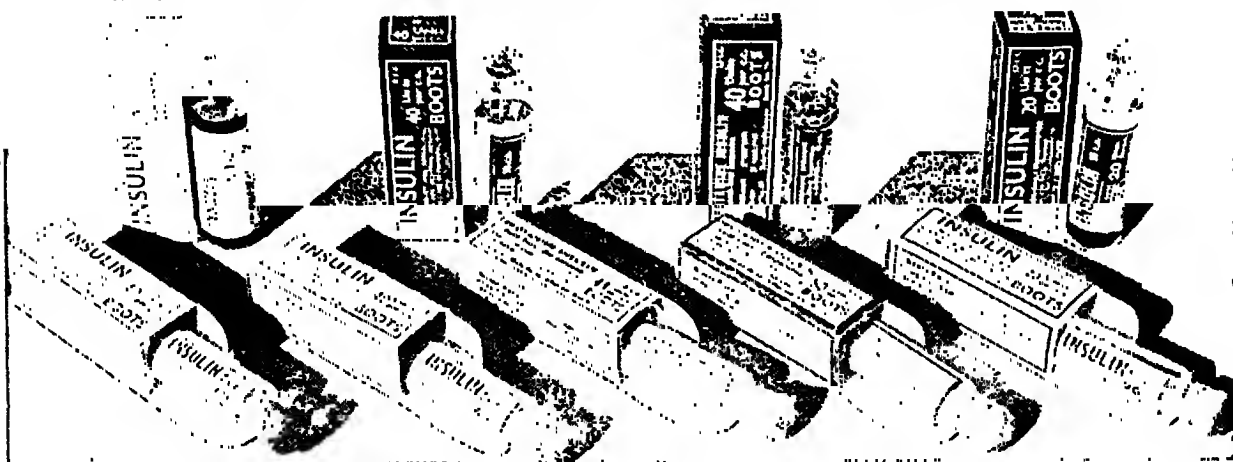
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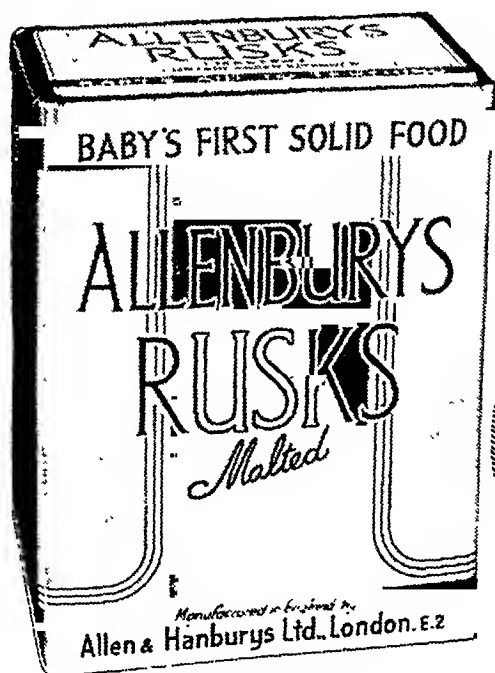
# Baby's First Food Solid

Allenburys Malted Rusks are a valuable food from the age of ten months onwards, and may be used even earlier as a stimulus to salivary secretion and a help to teething. Their use encourages the development of a strong, wide jaw in which there is ample room for the teeth.

Vitamin D (calciferol), in the form of irradiated ergosterol, is added to the Rusks in the process of manufacture, in order to ensure normal calcification of bones and teeth.

The Rusks retain their crispness and flavour under the most varied climatic conditions.

In tins containing  $\frac{1}{2}$  lb., 1 lb.,  $2\frac{1}{4}$  lbs.



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including all the most recent work in this line, especially as regards the thalamic nuclei.

The reader's attention is held throughout, owing largely to the author's aim to present the nervous system in its relation to the living organism.

The B. N. A. nomenclature has been used throughout with few exceptions. Some of the spinal tracts have been renamed and the old and B. N. A. nomenclature

given in brackets. It is doubtful whether this is really an improvement.

The book is well written and is a pleasure to read. It contains an extensive bibliography at the end. It can be confidently recommended to all who are interested in the study of the nervous system.

J. G.

## Abstracts from Reports

### BENGAL PUBLIC HEALTH REPORT FOR THE YEAR 1937. BY LIEUT.-COL. A. C. CHATTERJI, M.B., D.P.H., I.M.S., DIRECTOR OF PUBLIC HEALTH

DURING the year under review, the death rates from dysentery and diarrhoea, respiratory diseases and

Twenty-seven thousand, nine hundred and forty-four deaths were due to smallpox in the province in 1937 against 46,276 in 1936, yielding a death rate of 0.6 per mille against 0.9 in 1936 and 0.3 the mean of the previous quinquennium.

The total number of deaths reported from dysentery and diarrhoea in 1937 was 56,800 with a death rate

#### Fever deaths in 1936 and 1937

Causes	NUMBER		DEATH RATES PER MILLE		Percentage of increase + or decrease — in 1937	PERCENTAGE TO TOTAL FEVER MORTALITY	
	1936	1937	1936	1937		1936	1937
Malaria fever ..	337,647	372,992	6.8	7.5	+ 10.3	47.1	48.1
Enteric fever ..	8,359	8,978	0.17	0.18	+ 5.9	1.2	1.1
Measles ..	4,549	4,875	0.09	0.10	+ 11.1	0.6	0.6
Relapsing fever (spirochætal).	7	2	0.0001	0.00004	— 60.0	0.001	0.0003
Kala-azar ..	21,161	21,227	0.42	0.42	± 0.0	2.9	2.7
Influenza ..	2,502	2,422	0.05	0.05	± 0.0	0.3	0.3
Cerebro-spinal fever ..	910	938	0.02	0.02	± 0.0	0.1	0.1
Typhus fever ..	1,551	2,814	0.03	0.06	+ 100.0	0.2	0.4
Blackwater fever ..	115	229	0.002	0.004	+ 100.0	0.02	0.03
Other fevers ..	339,341	361,109	6.8	7.2	+ 5.9	47.4	46.5

injuries were the same as in the preceding year. There was reduction in the comparative rates in cholera and smallpox but in fevers and all other causes the rates

of 1.1 per mille against 57,212 with the same death rate in 1936. The death rate increased by 10 per cent against the last quinquennial average (1.0 per mille).

#### Respiratory diseases

Diseases	NUMBER		DEATH RATES PER MILLE		Percentage of increase + or decrease —	PERCENTAGE OF TOTAL DEATHS FROM RESPIRATORY DISEASES	
	1936	1937	1936	1937		1936	1937
Pneumonia ..	49,155	48,927	0.98	0.98	± 0.0	51.8	50.4
Pulmonary tuberculosis	15,266	14,668	0.31	0.29	— 6.5	16.1	15.1
Whooping cough ..	1,247	1,519	0.02	0.03	+ 50.0	1.3	1.6
Other respiratory diseases	29,149	31,872	0.58	0.64	+ 10.3	30.7	32.9

were higher than those of the previous year. There was no death from plague in the presidency during the year under review. The infantile death rate increased by 3.1 per cent in 1937 as against an increase of 7.8 per cent in 1936.

Cholera accounted for 32,710 deaths in 1937 yielding a death rate of 0.7 per mille against 76,100 deaths with a death rate of 1.5 per mille in the previous year showing a decrease as large as 53.3 per cent over the latter. It was also 30 per cent less than the average of the previous quinquennium (1.0). 2.6 per cent of the total provincial deaths in 1937 were due to cholera.

### ANNUAL REPORT ON THE WORKING OF THE CIVIL HOSPITALS AND DISPENSARIES IN THE PROVINCE OF ASSAM FOR THE YEAR 1938. BY COLONEL E. S. PHIPSON, C.I.E., D.S.O., M.D., F.R.C.P., I.M.S., INSPECTOR-GENERAL OF CIVIL HOSPITALS

FROM a detailed study of the working of the hospitals and dispensaries in this province, covering a period of rather more than eighteen months, I have arrived at certain conclusions which I now record.

The working of the hospitals and dispensaries in this province is handicapped to a serious extent in two



ways: firstly by the lack of nurses, and secondly by the lack of skilled medical attention.

The hospitals and dispensaries are, on the whole, reasonably well built and equipped, and many have excellent operating rooms, women's wards and special wards for private patients provided, it may be, by local benefactors, and yet comparatively little of the accommodation and facilities provided can be used for the purposes for which they are really intended because of the lack of trained nursing.

A subdivisional medical officer must of necessity think twice before he admits a serious medical case when he knows that the attention a case can receive at night is probably limited to the care that an over-worked compounder can give, and he knows he is taking a definite and sometimes unjustifiable risk when he operates, except from sheer necessity, in the absence of that skilled after-care which so often makes the difference between success and failure in surgical work. It is largely due to this, that surgical work in State and Local Board hospitals comprises so few 'selected' cases, a group which includes those cases in which relief is sought, but not urgently and imperatively required, and which, in properly staffed hospitals, ought to comprise the majority.

The solution to this problem lies, I think, in the practical recognition, by Government, by local bodies and by local benefactors, that the efficiency of a hospital is determined not only by the quality and sufficiency of its buildings and equipment, but also by the quality and sufficiency of its personnel, and that trained nursing is as much a part of a hospital unit as are doctors. Given the necessary funds, there should be no great difficulty in establishing a training school for nurses at the Dibrugarh Civil Hospital, and if suitable hostel accommodation is provided for them, there is good reason to believe that young women of the province, of the necessary educational standard, would be willing to come forward and undergo the course of training necessary to fit them for the career of a trained nurse in the hospitals of the province.

I have stated above that the other main defect is the lack of skilled medical attention. There are two main reasons for this: one is that, owing to financial stringency, the opportunities for self-improvement in a wider field which were formerly given to officers in the Assam Medical Service, on whose shoulders falls the bulk of the responsibility for medical relief of the people, have been denied to them for many years, and post-graduates study, which is universally recognized as an essential condition of medical efficiency, is now in abeyance without any apparent hope of resuscitation, with the inevitable consequence that the standard of efficiency throughout the service is steadily deteriorating. This is the more unfortunate when it is remembered that the Assam Medical Service, and particularly the senior branch of it, has the prospect of greater opportunities in the future than at any time in the past; and yet there are few indeed who are fitted for them, through no fault of their own.

The second reason for the lack of skilled medical attention (from the patient's point of view) is the constant and at times almost overwhelming pre-occupation of Government executive medical personnel, including civil surgeons and subdivisional medical officers, with duties, whether administrative, clerical or supervisory, which are encroaching in ever-increasing volume on the time during which the medical officer is actually able to function in a purely medical capacity, that is, in the healing of the sick. This is not to say that these duties are superfluous; they are, on the contrary, part of the necessary machinery of Government and departmental routine as at present organized, but I am convinced that if greater efficiency in actual medical relief is to be sought, the burden ought to be lightened or at least redistributed.

**Kala-azar.**—There were 8,775 cases and 112 deaths, against 6,712 and 66 deaths in 1937.

The following figures for the last eight years show the numbers treated in hospitals and dispensaries other

than those directly under the Public Health Department:—

1931	..	3,755	1935	..	5,476
1932	..	3,696	1936	..	5,327
1933	..	4,443	1937	..	6,712
1934	..	5,558	1938	..	8,775

The number of patients treated during 1938 was larger by 2,063 than that of 1937. The increases occurred in the Sibsagar, Sylhet, Cachar, Nowgong and Kamrup districts.

These figures call for more than passing notice. Allowing for the fact that during the past two years local surveys have been intensified, which would have the effect of bringing forward for treatment a number of cases which otherwise might have been undetected, the steady increase in cases treated in hospitals and dispensaries must be regarded as significant, the more so when it is recognized that the cases treated by the Public Health Department dispensaries show a corresponding increase, and still more so when the increase in kala-azar incidence in this province is considered in relation to the recent great increases reported in the incidence of the disease in Northern Bengal, Sikkim and the northern districts of Bihar. All these indications suggest the likelihood that the incidence of kala-azar may, before long, again assume epidemic proportions.

This is a prospect that cannot be regarded with complacency, since the unpalatable truth confronts us that, in spite of the huge sums, in the aggregate over 47 lakhs of rupees, spent on kala-azar in the last nineteen years in Assam, in no instance has the disease been stamped out from where it obtained a foothold in the 1925 epidemic; that no effective means of prevention, based on the true epidemiology of the disease, has yet been devised, and that in the present state of our knowledge we are almost powerless to prevent its spread, except by treatment. This method, although it is highly effective and although the medical personnel are highly organized and trained in its employment, is costly and ignores the earlier and perhaps the most vital links in the chain of causes which culminate in the infection of the individual. Briefly, we can cure an infection, once established, with great precision, but we cannot prevent its occurrence. It is in the attempt to fill the dangerous gaps in our knowledge of the disease, that the Indian Research Fund Association have recently authorized a special enquiry into improved methods of prevention and into the mode of transmission of the disease and the Government of Assam have been invited to contribute to the cost of the enquiry.

#### ANNUAL REPORT OF THE CHEMICAL EXAMINER TO THE GOVERNMENT OF MADRAS FOR THE YEAR 1938

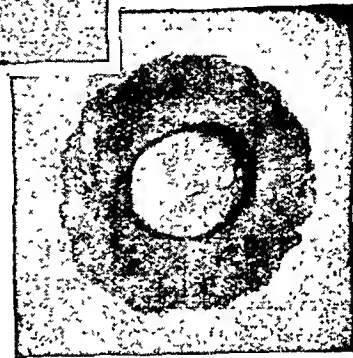
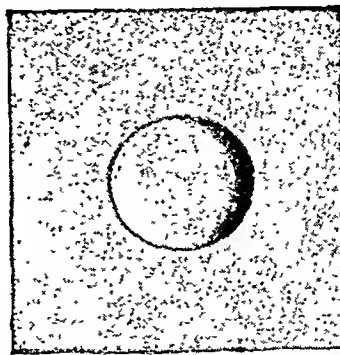
THE total number of human poisoning cases examined during the year was 467 with 2,485 articles as compared with 426 cases with 2,427 articles in 1937. Poison was detected in 241 cases or 51.6 per cent.

Datura heads the list this year with 36 cases followed by oleander with 30 and opium with 29 cases. There were 14 cases of madar juice poisoning. Cases of poisoning with organic poisons were nearly twice as frequent as those with inorganic poisons. Among the inorganic poisons, mercury claimed 21 cases, arsenic 20, copper sulphate 12, cyanide 10 and nitrite 9. There was a marked increase in datura and nitrite cases.

#### INTERESTING CASES

**Potassium bichromate.**—There are certain mendicants in this country who go about trying to impress people with their supernatural powers by undertaking to swallow anything from prickly-pear to poison. A man, probably of this type, came to a village and swallowed daily for some days about an ounce of sulphur drinking his own urine as 'antidote'. As the villagers did not

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phenolphthalein emulsion—has attained a reputation all its own.

Only the finest and purest ingredients are used in Agarol. Its exceptional palatability, secured without artificial flavouring, renders it acceptable to both children and adults. Agarol contains no alcohol and no alkali and, being devoid of sugar, is particularly suited to diabetic cases.

*A trial supply to Physicians on request.*

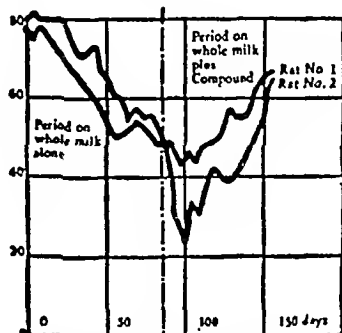
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**WILLIAM R. WARNER & CO. LTD.,**  
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# Anaemia yields readily

Results of experiments devised to determine the potency of Waterbury's Compound as a haemoglobin restorative in nutritional anaemia.



Haemoglobin count using the Dare Haemoglobinometer and scale. Sample taken from tail artery.

85th day, period when supplementing with Waterbury's Compound was begun.

## TO WATERBURY'S COMPOUND *PLAIN*

Anaemia is probably the most frequent after-effect of disease, and the most persistent. It will yield readily to intensive treatment with Waterbury's Compound.

This preparation contains fresh liver, spleen and cod liver oil, acted upon by digestive ferments for easy absorption and assimilation.

Waterbury's Compound is also supplied with Creosote and Guaiacol to make it more efficient at those seasons when coughs, colds, and respiratory ills need special attention and care.

May we send you a bottle of each form of this very palatable and dependable haematinic and reconstructive to form your own conclusions?

Made by Waterbury Chemical Co. Inc., New York  
and St. Louis, U.S.A.

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## Gastric Hyperacidity

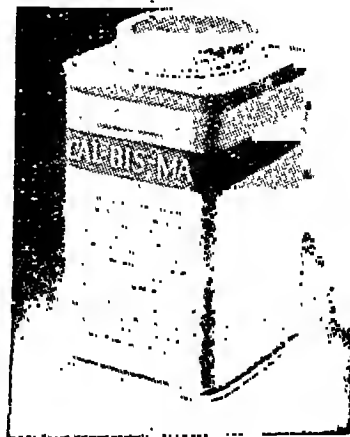
In the relief of gastric hyperacidity, *speed* is essential—Cal-Bis-Ma provides it. The neutralizing effect should be *prolonged* so as to prevent secondary acid rise—again Cal-Bis-Ma takes care of that. The irritated gastric mucosa should be soothed and protected from further irritation—that, too, is an important mission of Cal-Bis-Ma.

Send for a trial supply and descriptive literature.

# CAL-BIS-MA

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seem impressed with this show, he swallowed one day in their presence a substance stated to be 'red sulphur' and drank the usual 'antidote'. He collapsed and was removed to a hospital where he died one hour after swallowing the poison. We detected in his viscera chromium equivalent to about three hundred and twenty-nine grains of potassium bichromate and we found the remnants of the 'red sulphur' to be potassium bichromate weighing about three hundred and forty-two grains.

**Cyanide.**—An immoral wife had a child who was in the habit of eating out of the same dish with her husband. She left the child with her relations one morning and served to her husband food mixed with poison that night. After eating a few morsels he collapsed and died in about twenty minutes. The woman threw the remnants of the food outside the house where a stray dog devoured them and died almost immediately. The villagers promptly informed the police who sent us the viscera of the man, the viscera of the dog and the remnants of the suspected poison seized from the woman. We detected cyanide in the viscera of the man as well as in the viscera of the dog and we found the remnants of the suspected poison to be potassium cyanide. The woman stated at her trial that she had administered the substance as a 'love potion' to her husband. She was awarded the extreme penalty of the law.

**Chloroform.**—A young man was brought to a hospital in an unconscious state with dilated pupils and stertorous breathing, the breath smelling strongly of chloroform. He died five minutes after admission. In his pocket was a letter in which he stated that he had swallowed chloroform to end his life. We detected about fifty-seven grains of chloroform in his viscera.

**Sulphonal.**—A man presumably wanted to go to heaven by motor car. He got into his car and before starting, swallowed from a tumbler a hypnotic drug mixed with water. He then drove on till the drug had its effect and the car hit a telegraph post. The car was wrecked but the driver escaped injury, though the effects of the hypnotic lasted for two days. The police found a tumbler in the wreckage of the car and sent it to us. We detected sulphonal in the contents of the tumbler.

**Datura.**—A quack gave his patient a paste of leaves as a remedy for guinea-worm. The unfortunate patient became unconscious and died. We detected particles of datura leaf in the contents of the stomach of the victim.

**Malai vembu (*Melia Composita* Willd.).**—A man drank the juice of the bark of 'malai vembu', vomited once and died within about an hour and a half. The viscera, the vomit and a specimen of the bark were sent to us. We did not detect poison in the viscera but we obtained from the vomit a crystalline poisonous acid ether extract resembling the poisonous acid ether extract obtained from a specimen of the bark. The acid ether extract obtained from each produced convulsions and death in frogs similar to those produced by picrotoxin. Each of the extracts gave with a dilute solution of benzaldehyde in absolute alcohol and a drop of concentrated sulphuric acid (Melzer's test) a permanganate purple colour, whereas picrotoxin gives a red colour. Further, the above two extracts did not give any colour on treatment with potassium nitrate and sulphuric acid and mixing with excess of solid caustic potash, whereas picrotoxin gives a brick red colour with the test. The extract from the bark does not reduce Fehling's solution either before or after treatment with emulsion or hydrochloric acid.

**Jungle potato (*Manihot utilisima*).**—The 'jungle potato' is stated to be in extensive use in Malabar and Cochin as a food, and according to local information there are stated to be two varieties, one poisonous and the other non-poisonous, without any appreciable difference between the two, except that the poisonous variety is darker with its leaves redder and cooks less soft than the non-poisonous variety. According to the local medical officer there have been instances of goats dying after eating the leaves of the poisonous variety

but no instances are known of human beings having been poisoned by eating the cooked root of the poisonous variety.

A woman and two children were stated to have died after eating the uncooked 'jungle potato'. Their bodies were in a state of advanced decomposition. The examination of the viscera which were sent to us did not reveal cyanide or other poison. The root which was suspected to have caused death was also sent to us. We identified it to be *Manihot utilisima*. When the fresh root was crushed and distilled after acidifying with phosphoric acid, hydrogen cyanide was detected in the distillate, the total quantity of hydrogen cyanide corresponding to about fourteen parts per hundred thousand parts of the root. The poisonous nature of this root would therefore appear to be due to the presence of a cyanogenetic glycoside. About a pound of the root eaten in the raw state would probably prove dangerous to human life.

#### THE REPORT OF THE CHEMICAL EXAMINER TO GOVERNMENT, PUNJAB, FOR THE YEAR 1938

THIS year 4,095 cases were examined as compared with 3,871 in the year 1937, giving a net increase of 224 cases. The exhibits examined, however, showed a decrease of 190 from 11,905 in 1937 to 11,715 during the year under report, but this is accounted for by the smaller number of samples of cocaine received for examination. As usual the increase in cases was mainly in the number of 'stain cases'. Human poisoning and cattle poisoning showed a substantial decrease. The percentage of detection showed an increase under all human poisoning, cattle poisoning and blood-stain cases. Opium, datura, arsenic and alcohol were, as usual, the principal poisons used in cases of human poisoning; while in cases of cattle poisoning the poisons used were arsenic and strychnine only. Lahore was again responsible for the largest number of human poisoning cases (69) followed by Delhi (39), Phillaur (30), Amritsar (29) and Ferozepore (21); while most of the cattle poisoning cases were received from Lahore Cantonment, Rawalpindi and Lahore, viz, 11, 10, and 8, respectively.

Of the 2,406 articles examined under the head 'General Analysis', 1,947 were excisable articles. The rest included 72 samples of drugs sent by the Medical Store Depot, 59 samples of ghee, of which only 27 were found to be fit for human consumption and 23 samples of water, of which 18 were found to be fit for drinking purposes.

During the year under report a three months' course of lectures by the Chemical Examiner to police inspectors has been inaugurated. It is hoped that this training will help them in estimating medico-legal evidence more scientifically at the scene of a crime and in selecting and despatching material for further examination.

#### ANNUAL REPORT OF THE CHEMICAL EXAMINER TO GOVERNMENT, UNITED PROVINCES AND CENTRAL PROVINCES, FOR THE YEAR 1938

##### HUMAN POISONING

THE total number of cases examined under this head was 427. Poison was detected in 67.0 per cent of cases as against 63.9 for 1937. The work was done more efficiently than would be apparent from these figures. A large number of unsatisfactory cases are sent up for examination every year and the paragraph 868 of the Manual of Government Orders often remains a dead letter. The forwarding officers should be directed to be more careful and to send for investigation only those cases where there is reasonable ground for suspecting that poison may have been the cause of death.

Datura was again the most commonly used poison. It was detected in 31.8 per cent of the detected cases.

Opium, arsenic, aconite, mercury, bhang, cyanides, alcohol, and nux-vomica (strychnine) came in order of frequency forming 27.2, 21.0, 3.8, 2.8, 2.4, 1.4, 1.2, and 1.1 per cent respectively of the detected poisons. Other inorganic poisons were detected in 2.4 per cent of the detected cases and other organic poisons in 4.9 per cent of the detected cases.

In 2.1 per cent of cases (26 articles), unidentifiable organic poisons were found. This shows the need for research on the indigenous vegetable poisons.

In 214 cases, including seven cases of abortion, viscera were received. Poison was detected in 60.3 per cent of these cases as compared with 57.5 per cent for the year 1937. This low percentage of detection is mainly due to the fact that a large number of cases were received in which the cause of death was other than poisoning. In 62 cases the death was obviously due to causes like drowning, serious multiple injuries, hanging, snake bite, fracture of skull, strangulation, heart failure, prolonged illness and pneumonia. Excluding the above the percentage of detection was 84.9 as compared with 85.4 for the year 1937.

In 42 fatal cases no post-mortem report was received and in 102 cases in which post-mortem reports were received no definite opinion was given as to the cause of death. In 31 cases two or more reminders had to be sent for the post-mortem reports. In 13 cases, traces of extraneous mercury were detected in the stomach washes and in 11 cases manganese was detected in the stomach washes, obviously because of the neglect of the directions given in circular no. 293 of 1936, dated the 11th November, 1936.

#### ANNUAL REPORT ON THE BERRY-WHITE MEDICAL SCHOOL, DIBRUGARH, FOR THE YEAR 1938-39

THE number of sanctioned beds has remained the same as in the last report (131) and the daily average of in-patients has risen from 98 to 110. This number is still far below what it should be in relation to the number of students.

The school staff has been slightly strengthened by the appointment of a laboratory assistant who has passed the I.Sc. Examination of Calcutta University, but the facilities for the teaching of practical chemistry and physics are in great need of improvement.

Lieutenant-Colonel Allen reports an increase in the number of labour cases conducted in the hospital from 46 to 50, and that the number of cases of diseases of women treated has increased from 139 to 391, an increase of nearly 200 per cent. This is attributed to the increasing popularity of the Narsingdas Jallan Maternity and Gynaecological Wards, and this is a very satisfactory feature of the report.

The number of microscopes remains the same as last year when the stock was re-inforced by the purchase of twenty new ones, but still more are needed.

An important innovation during the year under report was the admission, for the first time, of female students. In the past Government have provided for the medical education of a certain number of female students by the grant of scholarships tenable at the Campbell Medical School, Calcutta, at an annual cost of about Rs. 3,859. At first glance it appears reasonable, as a measure of economy, to save the greater part of this large sum by abolishing the scholarships tenable in Calcutta and substituting scholarships tenable at the Berry-White Medical School. As matters stand, with no hostel accommodation of any kind, there can be very few female students who, unless they have relatives in Dibrugarh, could make arrangements which would be satisfactory to their parents and the condition imposed must inevitably act as a bar to the acceptance of a scholarship or a seat by a student who might otherwise be in every way eligible to undertake the course.

Funds did not permit of any of the long list of necessary improvements being taken in hand during the past year, and the current year's budget allotments will permit of very few of the school's long-standing requirements being met.

#### ADMINISTRATION REPORT OF THE DIRECTOR OF MEDICAL AND SANITARY SERVICES, CEYLON, FOR 1938

THE Malaria Control and Health Scheme during 1938 continued to operate in the same areas as in 1937.

During the year under review the work of all the groups has functioned on one basis, viz, that of the health unit. This was made possible by smaller areas being assigned to both district medical officers of health and field medical officers.

A new departure is the placing of the dispensaries in charge of apothecaries under the supervision of medical officers of health and field medical officers. Dispensaries are field institutions dealing chiefly with malaria and ankylostomiasis and by right should come under the supervision of the health staff whose two chief problems are these diseases. By this procedure it is proposed to change the functions of the dispensary from a place for the mere dispensing of medicines to a centre for all rural health work of the area. It will be a centre for health propaganda and for conducting various types of clinics, such as ante-natal and baby welfare, school clinics, *parangi* clinics in centres where the disease occurs, and venereal disease clinics. Special emphasis is being placed on the effective treatment of malaria with all available drugs.

A type of work that has been developed during the year for villages in backward areas is for the medical officer of health or field medical officer of the area to visit them once a month, look up all expectant mothers, infants, pre-school and school children and attend to any conditions that need advice and treatment. Treatment for malaria, hookworm and yaws is given and those needing hospital attention are referred to the nearest hospital and the village headman makes himself responsible for seeing that they go to hospital. The transport of expectant mothers and destitute cases are met from Government funds. Instructions are left for any treatment before the next visit, to be obtained from the nearest dispensary. Steps are also taken to educate them in health matters by visits to homes, talks, and lantern and cinema shows. The people are encouraged to keep their gardens clean, to store their refuse in pits, to boil their drinking water, to develop a vegetable garden, to provide windows for their houses and to get rid of mosquito-breeding places. After their confidence has been secured by relieving them of some of their physical handicaps through treatment, the construction of latrines is undertaken. If taken up earlier the response may not be satisfactory. The people are getting interested in this type of work.

With the establishment of cottage hospitals the policy that is being followed is for the medical officer in charge to be given an area around the hospital for health work as well. The sanitary assistants and midwives in these areas are placed under the supervision of the medical officer. This same policy is being followed in the case of the smaller hospitals and dispensaries in charge of medical officers. During the year, work on this basis was established at two cottage hospitals, one small hospital, and one dispensary.

Control of soil pollution received adequate attention during the year and 27,244 latrines (21,792 in 1937) were built.

In the provision of protected water supplies 61 new public wells and 746 private wells were constructed and 3,735 wells were improved.

There have been nine cases of human plague, the lowest number in any year since the introduction of the disease into Ceylon. There have been no outbreaks in the provinces. The last case of plague occurred on 23rd August so that Colombo has been free of human as well as rat plague for a continuous period of four months and seven days. This freedom is assigned to the energetic measures taken in fumigating all grain and contact cargo arriving from plague-infected ports. There have been no cases of cholera or smallpox, which when they occur are introduced from India. The incidence of typhoid and dysentery continues to maintain its high level. Two thousand two hundred and two

# The Influence of Virol on the Growth of Children

*A Summary of Investigations\* published in the  
"Medical Officer," March 30 and April 6, 1935*

A NUMBER of children, all receiving their customary home diet, were given either No Supplement, Cod Liver Oil, Halibut Liver Oil (with milk to provide equal calories) or Virol. The experimental scheme provided that each child should have a period on each treatment in turn, in such a way that every possible sequence was included. Rigid statistical control was thus possible.

## Gain or Loss in Weight on Various Supplements :—

Supplement	Total gain in ozs. over all periods	Average gain per child per week in ozs. over all periods	Total loss in ozs. during summer period only	Average loss per child per week in ozs. during summer period only
No Supplement - -	88	0.3	— 103	— 1.4
Cod Liver Oil - -	287	1.0	— 77	— 1.1
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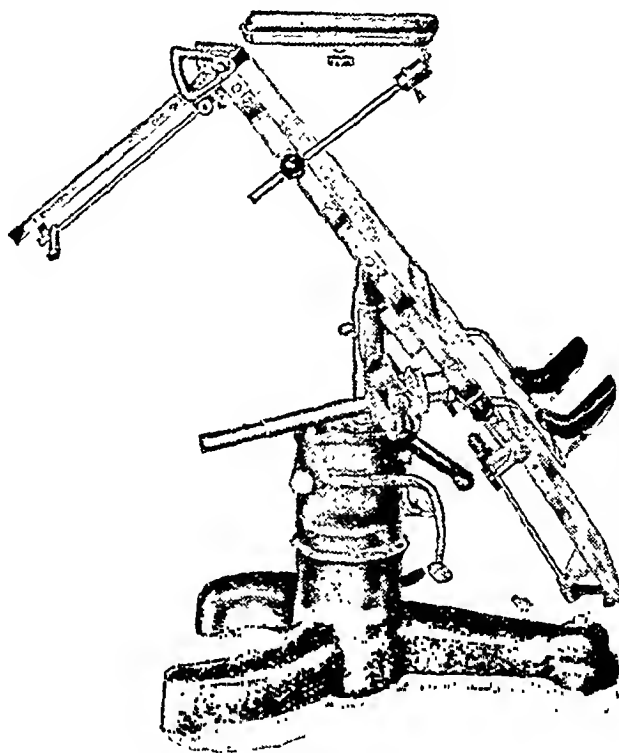
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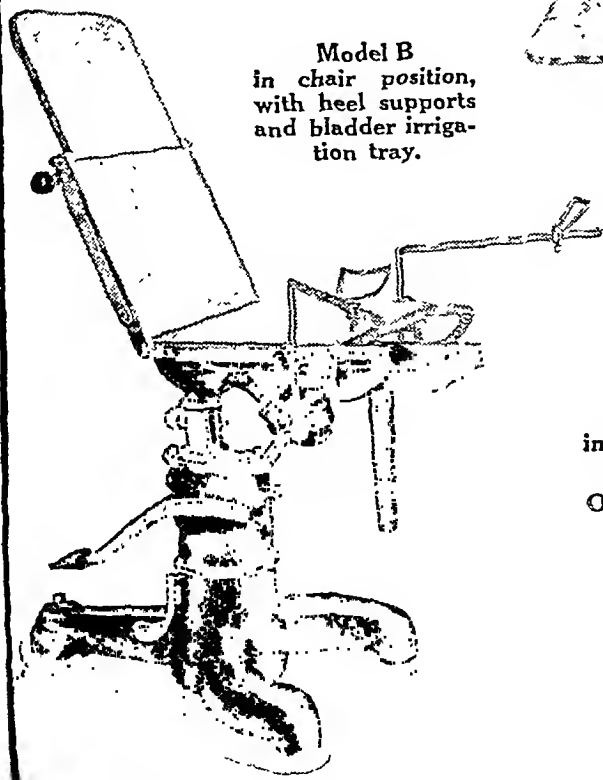
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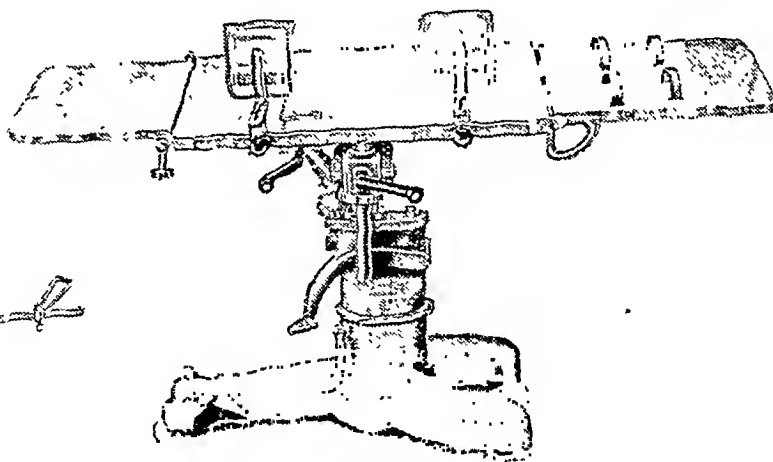


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cases of the former and 4,989 of the latter being reported. The control of these diseases depends on the more wide provision of latrines and protected water supplies. The incidence of diphtheria which is sporadic continues to show an increase from 135 in 1937 to 165 in 1938.

The incidence of malaria during the year showed no increase. In many localities it was below the normal for the previous five years. The island-wide organization established as the result of the 1934-35 epidemic has functioned well in keeping the disease under control.

The hookworm campaign carried out 2,169,931 treatments.

The leprosy campaign which has completed its survey and organized its control work in the Eastern, Western, Sabaragamuwa and Southern Provinces completed the North-Western, North-Central and Central Provinces, and carried out follow-up work in provinces completed in previous years. At the end of the year there were 1,002 cases segregated at the two asylums, and 1,517 cases outside on parole.

The island-wide survey of filariasis completed the North-Western and Southern Provinces. The demonstration in filariasis control in Dewameddi Hatpattu in the North-Western Province was continued. Regulations for the control of the disease are before the Executive Committee of Health for their approval.

The control of yaws has been placed on a satisfactory basis and the work was well organized during the year by each medical officer of health and field medical officer surveying all cases in his area and recording and treating them. All contacts are also noted and both cases and contacts are looked up and treatment given to those needing it every six months.

Maternity and child welfare work continues to be popular. The work was carried out at 311 centres as compared with 207 in 1937; 9,485 clinics were held as compared with 8,375 in 1937, with a total attendance of 76,108 expectant mothers as compared with 39,841 in 1937, 157,988 infants as compared with 88,479 in 1937 and 75,177 pre-school children as compared with 39,637 in 1937. In spite of this increased work it is rather disconcerting to find an increase in the infant mortality rate from 158 in 1937 to 161 in 1938 and in the maternal mortality rate from 19.9 in 1937 to 20.1 in 1938.

The number of schools in which health work has been done increased from 3,106 in 1937 to 3,461 in 1938; the number of children medically inspected increased from 84,730 in 1937 to 94,648 in 1938; the defects found were 173,071 compared with 124,540 in 1937; and the defects treated were 73,340 or 42.4 per cent compared with 36 per cent in 1937. School health education has received greater interest and support.

#### REPORT OF THE EUROPEAN MENTAL HOSPITAL AT RANCHI FOR THE YEAR 1938. BY MAJOR MOORE TAYLOR, M.D., D.P.H., I.M.S., MEDICAL SUPERINTENDENT

An endeavour has been made to keep in touch with and practise all modern methods of treatment. Those methods which have proved beneficial in the past, and which have been fully described in previous reports, e.g., prolonged narcosis, pyrexial and malarial therapy, hydrotherapy, etc., are continued, and need no further description.

During the year under report, 44 patients were discharged as cured—the ratio per cent of cures to direct admissions being 42.88. This represents an increase of 11.03 per cent as compared with the rate in 1937, and an increase of 27.42 as compared with the rate in 1936.

Of 44 patients discharged as cured, 24 who suffered from schizophrenia were treated by shock therapy. Three methods of treatment were employed—(1) Cardiazol therapy alone, (2) Cardiazol therapy combined with insulin, (3) Cardiazol therapy combined with pyrexial therapy (sulfosin). Three patients who suffered from schizophrenia were discharged as

'improved', all of whom received treatment by the cardiazol method combined with pyretotherapy.

Convulsion therapy was not successful in all cases in which it was administered. In 13 patients there was no improvement, in 10 patients there was improvement—but the mental condition after treatment did not warrant their appearance before the committee of visitors, with a recommendation for discharge. In seven patients the treatment had to be discontinued as the mental symptoms appeared to be aggravated, but in no case was the treatment followed by any alarming physiological result.

My own experiences of convulsion therapy during the first six months of 1938 were published in the *Indian Medical Gazette* (October 1938). Statistics are now available from nearly all European and extra-European countries covering upwards of 4,000 cases. These show that full remissions can be achieved in 50 per cent of recent cases (duration of illness 12-18 months). The prospects of success diminish in ratio with the length of duration. The treatment has been given to all new admissions in this hospital, and all other cases in the hospital which were suitable for treatment were given a trial, no matter what the duration of the illness.

The cases classified as 'improved' were those in which gross schizophrenic symptoms were manifested, but in much milder forms. Marked ameliorative changes occurred in the clinical status of this group both during and after treatment, and some, for the first time in years, became capable of doing productive work.

The cases classified as 'not improved' were those who showed no essential change in their hospital status, or those who presented evidence of intensification of symptoms.

The small number of cases makes it impossible to evaluate sex differences, but from the results obtained it would appear that treatment by the method is more beneficial in males than in females. The study of the subject is still being continued in this hospital, and it is hoped to publish later a detailed critical analysis of the work which is being carried out. The ultimate value of this form of treatment will of course be determined by the degree of permanency of improvement.

It was found in some cases that the action of cardiazol is enhanced by small doses of insulin, and in such cases we administer from 20 to 50 units of insulin, subcutaneously, two hours before the cardiazol injection, and the convulsions appeared to occur with greater facility. There is no doubt that the introduction of shock therapy has brought about an increased interest and enthusiasm in psychiatry. The results have amply justified this method of treatment. It is safe, and can be used in private practice and even at home.

*Insulin method of shock therapy.*—The literature on the insulin shock therapy of Sakel has been extensive. In this hospital the method has not been used extensively. Insulin cases require careful and constant supervision, and it takes a long time to learn the intricacies of the method. The treatment requires hospitalization and nursing of the highest type. Physicians must be in constant attendance. The literature indicates that in about 7 per cent of the cases of insulin shock, early termination of the coma may be necessary because of alarming signs and symptoms. Among these complications and dangers are vomiting, aspiration of saliva, vasomotor collapse, spasm of the glottis, tachycardia, cyanosis, prolonged extensor spasms, epileptiform convulsions, and after-shock or even status epilepticus, which may occur in spite of an adequate carbohydrate intake.

It is claimed that with insulin therapy the best response is obtained with hebephrenic and paranoid cases exhibiting an acute onset with marked symptomatology and hallucinations. With care, the complications likely to occur with the insulin method can be reduced to a minimum, and it is not suggested that there is any advantage of cardiazol therapy over insulin therapy, but when the staff is barely sufficient to meet the ordinary needs of the hospital, one is compelled to

give preference to cardiazol therapy—but I should have liked to have tried by the insulin method all cases where there was failure by cardiazol therapy.

The treatment of schizophrenia by the cardiazol method is, however, so much easier and less costly to administer than the insulin method, that it is urgently desirable to establish its value and limitations.

*General paralysis of the insane.*—Two patients in the early stage of this disease who had complete remissions were discharged, and were able to resume their normal activities. The method of treatment used in both cases was a combination of tryparsamide and malarial therapy. Three patients in an advanced stage of general paralysis showed no improvement with this treatment.

Occupational therapy continues to be the chief adjunct to other methods of treatment. It is a means of treating patients in the early stages of disease and in convalescence, and even those whose condition is considered irrecoverable. In many cases recovery is hastened and in others institutional life is made more pleasant. The department continues to make all uniforms of ward-boys, *ayahs*, and menial staff, most of the patients' clothing, and all ward furniture. The interest which the patients obtain from a mere change of environment for the time being, from seeing others doing good and interesting work, and more especially from the personal experience that they can do something useful, is of great value. They acquire a new outlook, and gain self-confidence, and these, in many cases, are the beginnings of a larger usefulness to the general community. In the occupational department patients are allowed to select their own work as far as possible. This is important, because what appeals and acts as a stimulus to one may not affect another. They may be engaged in the making of rugs, raffia and cane baskets, trays, weaving, needlework, designing, painting, book-binding, and in metal, leather and woodwork. The classes in cookery are popular with both sexes.

We have not yet developed a reasonable expectation of recovery in any type of mental disease, but even if that day does arrive, there will still be a large residue of patients for whom specialized care must be provided during the remainder of their days. To these the institution is home. They form a real community and their fundamental needs—food, shelter, work, play, friendship—can only be met in an institution of this description. The climate here is such that all patients, except the few confined to bed, or on special treatment, are out of doors and about the grounds, engaging in activities ranging from strolling to highly-organized and competitive games.

The patients assisted by the staff staged a number of excellent concerts during the year, and parties attended the cinema at Ranchi, whenever suitable films were being shown. The social evenings and dances continue, and a full Christmas programme was brought to a close with the usual New Year's Eve Fancy Dress Ball.

The daily classes under a qualified instructor are greatly appreciated by both male and female patients.

#### THE REPORT ON THE WORKING OF HOSPITALS AND DISPENSARIES IN THE PUNJAB FOR THE TRIENNium 1935-37

In spite of the financial stringency and economic depression the activities of the medical department during the triennium 1935-37 were not restricted. The triennium opened with 961 dispensaries (687 in rural and 274 in urban areas) and closed with 968 (693 in rural and 275 in urban areas). The total number of State Public Hospitals in the Province at the close of the year 1937 was 53 as compared with 51 in 1936 and 50 in 1935.

There were 364 rural dispensaries including nine subsidized dispensaries functioning in the province on the 31st December, 1937, *viz.*, 360 out of 375 provided under the 1925 scheme for expansion of medical relief in rural areas, and four maintained by district boards. The difference in the annual cost of maintenance of these two classes of dispensaries is considerable;

Government have decided that in future the expansion of medical relief in rural areas should be by means of opening subsidized dispensaries. As at present organized, a rural dispensary serves only a few villages in the immediate vicinity. To increase the usefulness of these dispensaries and to bring modern medical relief within easy reach of villages, it is essential under present conditions, when very few private practitioners have settled in the rural areas, that doctors in charge of rural dispensaries should periodically visit large villages within their areas. A beginning has been made in this direction and a scheme under which medical officers of rural dispensaries are required to tour in the surrounding villages has been successfully tried in selected *tahsils* of 23 districts.

As compared with the last year of the previous triennium 1932-34, the total number of patients treated fell by 165,571 in 1935, but increased by 619,920 in 1936 and by 715,668 in 1937. The decrease in 1935, which was in the number of out-patients only, was due to a lower incidence of malaria in that year. There was, however, a steady increase in the number of in-patients, *viz.*, 6,050 in 1935, 6,956 in 1936 and 16,300 in 1937 as compared with the figures for the year 1934. The principal diseases during the triennium under review were malaria, dysentery, cataract, pneumonia, influenza, enteric fever and tuberculosis. The total number of surgical operations performed rose from 569,671 in 1934 to 592,442 in 1935, 606,720 in 1936 and 630,969 in 1937. This steady increase in surgical work is a sure indication of the growing popularity of hospitals and dispensaries. Government have read with pleasure the names of the medical officers mentioned in paragraph 25 of the report who performed the largest number of surgical operations, mainly cataract extractions.

In addition to the five leper homes, managed by the mission organizations and subsidized by Government and the Punjab Branch of the British Empire Leprosy Relief Association, there are 100 leprosy out-door clinics in the province. Accommodation in these homes is, however, becoming inadequate, partly as the result of non-infectious cases remaining at the homes and partly owing to the large number of lepers coming from places outside the Punjab.

The scheme inaugurated in 1925 for providing medical aid to women by lady assistant surgeons in separate hospitals at each district headquarters and by women sub-assistant surgeons at each *tahsil* headquarters has not so far been completed. During the triennium under review seven new women's hospitals or sections were opened involving an addition of one woman assistant surgeon and six women sub-assistant surgeons to the existing cadre, which now consists of 10 women assistant surgeons and 55 women sub-assistant surgeons. There is, however, still one district headquarters, namely, Jhelum and 52 *tahsil* headquarters in the province which are without a lady doctor.

Medical education among girl students is becoming increasingly popular, so much so that many are refused admission in medical colleges and schools for want of accommodation. During the triennium under review 127 midwives, 189 nurse *dais* and 1,056 trained *dais* qualified themselves for the diploma and certificates of the Punjab Central Midwives Board.

The schemes for the medical inspection of school children both in rural and urban areas, and the anti-rabic work at the provincial centre at Lahore and also at district and *tahsil* headquarter hospitals continue to function satisfactorily.

#### ANNUAL REPORT ON THE WORKING OF THE PUNJAB MENTAL HOSPITAL, LAHORE, FOR THE YEAR 1938

The total number of patients treated in the hospital rose from 1,153 (923 males and 230 females) in 1937 to 1,235 (988 males and 247 females) in 1938. The number of patients admitted during the year was 254 (208 males and 46 females) as against 162 (139 males and 23 females) in the previous year.

The number of patients discharged from the hospital was 166, *viz.*, 84 'cured', 30 'improved', 34 'not

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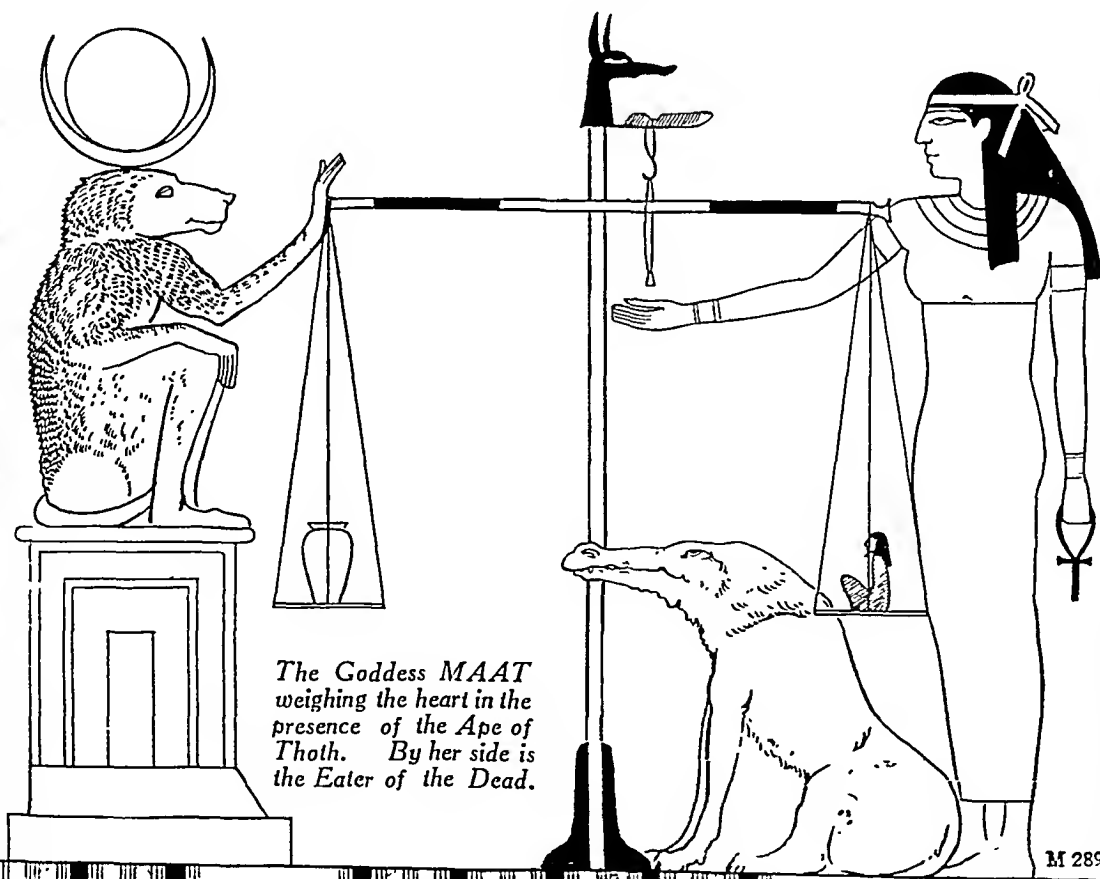
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improved' and 18 'otherwise' as compared with 143, viz, 58, 25, 52 and 8, respectively, in 1937.

The total number of deaths was 32 in 1938 and 29 in 1937. Of 32 deaths in 1938, 6 were due to pneumonia, 5 to tuberculosis of the lungs, 2 each to ankylosoma, debility, dysentery, diarrhoea and epilepsy and the remaining 11 to various other causes.

Of the total number treated in the hospital during the year 216 (211 males and 5 females) were criminal patients. The year 1938 opened with 150 criminal patients, 62 were admitted and 4 re-admitted during the year, 43 were discharged or transferred and 6 died.

The existing accommodation in the hospital both for male and female patients is not adequate. New barracks for 300 additional male patients are now ready and will be occupied as soon as the additional staff for which the sanction of Government has been applied for is provided. The project of a double storeyed block for 100 additional female patients has been sanctioned.

In 1938 special forms of treatment by cardiazol and insulin were introduced and very promising results were obtained. Out of 94 patients treated 27 were cured and 31 improved. Owing to the shortage of funds it was not possible to try the experiment on a large scale.

#### ANNUAL REPORT ON THE WORKING OF THE CIVIL HOSPITALS AND DISPENSARIES IN THE MADRAS PRESIDENCY FOR THE YEAR 1938

The number of medical institutions of all classes in the Province increased from 1,283 in 1937 to 1,322 in 1938. This was mainly due to the increase in the number of private-aided institutions from 79 to 115 and of subsidized rural dispensaries from 404 to 416. The total number of in- and out-patients increased from 280,150 to 310,030 and from 17,179,284 to 18,692,411 respectively. The percentage of deaths to the total number treated decreased from 4.79 to 4.62.

**Tuberculosis.**—The Tuberculosis Institute at Egmore, the Tuberculosis Hospital at Royapet, the Tuberculosis Clinic in the Victoria Caste and Gosha Hospital, Madras, and Tuberculosis Sanatorium at Tambaram did good work during the year under review. The number of patients treated for tuberculosis increased from 76,915 to 85,799. The tuberculosis clinic run by the King George Thanksgiving Fund continued to be in charge of contact examination. In December 1938 a ward of ten beds for women was constructed at the Tambaram Sanatorium out of His Excellency the Viceroy's Entertainment Fund and was handed over to the Government. The Government have permitted private patients to construct cottages at the sanatorium.

**Leprosy.**—Anti-leprosy work continued to make steady progress. The number of leprosy clinics increased from 442 to 456 and the total number of cases treated increased from 62,228 to 62,751. Leprosy officers carried out survey work in 82 villages. Students numbering 24,139 in 157 schools were examined and 389 cases of leprosy were detected.

**X-ray department.**—There was a large increase in radiological work (159,543 sittings as against 119,543 in the previous year) in the Barnard Institute of Radiology, Government General Hospital, Madras. Six medical officers were trained at the Institute.

**Medical services.**—In accordance with the scheme for the appointment of honorary medical officers in Government medical institutions, seven posts of civil assistant surgeon were thrown open to honorary officers and steps are being taken to accelerate the appointment of honoraries to more paid posts.

## Correspondence

### COOLEY'S ERYTHROBLASTIC ANÆMIA

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I was interested to read a case report of Cooley's anæmia by Napier and others in your issue of the current month [the paper appeared in the November number]. I had come across two cases of this condition at the B. J. Hospital for Children, Bombay, under the care of Dr. G. Coelho.

Two such cases were demonstrated by Dr. G. Coelho at the J. J. Hospital Post-Graduate Clinical Union meeting held on 17th March, 1939, and published in the *Medical Bulletin* of 6th May, 1939.

Detailed accounts of these same cases were reported by me at a meeting of the Teaching Pathologist held on 17th June, 1939, at Bombay. Accounts of this meeting had appeared in the *Medical Bulletin* of 2nd September, 1939.

Yours, etc.,  
J. G. PAREKH, M.R.C.P.,  
Honorary Assistant Physician.

J. J. HOSPITAL,  
BOMBAY,  
15th December, 1939.

[Note.—We are afraid that we overlooked the account of these two cases of Cooley's anæmia that appeared in the May issue of *Medical Bulletin*: the second report had not come into our hands when we sent our account of this case to press.

There seems to be little doubt that Dr. Coelho's cases were also Cooley's anæmia, though the bony changes in the skull were not nearly so characteristic as in our case.

Another case, also from Bombay, was reported in the October number (received late in November) of the *Indian Journal of Pediatrics*; again the bony changes are not so marked but are certainly suggestive.

The fact that four cases have been diagnosed in so short a time, in two centres in India thirteen hundred miles apart, suggests that the disease is not uncommon in this country, and adds support to the editorial remark in our last issue, namely, that few diseases are peculiar to one locality or to one racial group.—L. E. NAPIER.]

## Service Notes

### APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL G. G. JOLLY, C.I.E., V.H.S., Officiating Director-General, Indian Medical Service, is confirmed in his appointment, with effect from the 8th November, 1939.

Colonel (now Major-General) G. G. Jolly, C.I.E., V.H.S., is appointed Honorary Physician to The King, 17th August, 1939, vice Lieutenant-Colonel (Brevet-Colonel) R. N. Chopra, C.I.E., retired.

Colonel J. Taylor, C.I.E., D.S.O., V.H.S., is appointed Honorary Surgeon to The King, 30th August, 1939, vice Colonel Sir Alexander J. H. Russell, K.C., C.B.E., retired.

Lieutenant-Colonel J. L. D. Yule to be O. C., C. I. M. H., Dehra Dun. Dated 14th November, 1939.

Lieutenant-Colonel A. D. Loganadan is appointed as a leave reserve officer in the Central Indian Medical Service Cadre and is posted to the Office of the Director-General, Indian Medical Service, with effect from 8th December, 1939 (afternoon).

His services are placed at the disposal of the Government of Bombay, with effect from the 12th December, 1939 (afternoon).

Lieutenant-Colonel Jelal M. Shah, M.B.E., has been appointed as Superintendent of Mahabaleshwar, with effect from the forenoon of 14th December, 1939.

On reversion from foreign service under the I. R. F. A., Captain T. Sommerville has been appointed a leave reserve officer in I. M. S. Cadre under the



Central Government, with effect from the afternoon of the 28th September, 1939.

Captain G. W. Miller is appointed as a leave reserve officer in the I. M. S. (Civil) Cadre under the Central Government, with effect from the 4th October, 1939 (forenoon), and until further orders is posted to the Port Health Department, Bombay.

Captain J. White made over charge of the Midnapore Central Jail to Major B. Chowdhury, on the forenoon of the 4th November, 1939.

Captain P. I. Franks is appointed to be Surgeon on the personal staff of His Excellency the Governor of Bengal, with effect from the 18th November, 1939.

Captain T. E. Palmer, O.B.E., was transferred to Civil employment in Madras. Dated 19th November, 1939.

Captain W. A. N. Marrow was transferred to Civil employment in Madras. Dated 24th November, 1939.

Captain D. W. Taylor, officer on special duty at the Mayo Hospital, Lahore, assumed charge of the office of Civil Surgeon, Ambala, on the 1st December, 1939, forenoon.

Captain R. L. Raymond, Civil Surgeon, Magwe, was posted for duty to the Defence Department as Special Officer to conduct a survey of 'goitre' in the Chin Hills. He relinquished charge of his duties as Civil Surgeon, Magwe, on the forenoon of 22nd December, 1939.

#### LEAVE

Lieutenant-Colonel R. C. Wats, Assistant Director, Haffkine Institute, Bombay, has been granted leave for 1 month, with effect from the forenoon of 3rd January, 1940, with permission to prefix the Christmas and New Year's day holidays to the leave.

Lieutenant-Colonel C. J. Lodge-Patch, M.C., Superintendent, Punjab Mental Hospital, Lahore, who was on leave *ex-India* till the 12th October, 1939, has been granted by the High Commissioner for India an extension of leave for six months.

Lieutenant-Colonel S. Nag was granted leave *ex-India* for the period from the 24th November, 1937, to the 9th April, 1939.

Previous notification is hereby cancelled.

Lieutenant-Colonel K. S. Thakur, Civil Surgeon, 24-Parganas, was granted leave for the period from the 26th April, 1938, to the 25th May, 1939.

Previous notification is hereby cancelled.

#### PROMOTIONS

Colonel G. G. Jolly, C.I.E., K.H.P., promoted to the rank of Major-General, with effect from the 8th November, 1939.

#### *Lieutenant-Colonel to be Colonel*

H. S. G. Haji, M.C. Dated 22nd October, 1939, with seniority from 25th July, 1935.

#### *Majors to be Lieutenant-Colonels*

P. A. C. Davenport. Dated 22nd October, 1939.

D. P. Bhargava, O.B.E. Dated 5th December, 1939.

Brevet Lieutenant-Colonel A. H. Craig. Dated 23rd December, 1939.

#### *Captain to be Major*

W. J. Moody. Dated 6th December, 1939.

#### *Lieutenants (on probation) to be Captains (on probation)*

W. M. McCutcheon. Dated 27th September, 1939, with seniority from 1st May, 1939.

W. D. P. Griggs. Dated 19th October, 1939, with seniority from 1st May, 1939.

D. S. Wilson. Dated 1st November, 1939.

#### RETIREMENTS

Colonel W. A. M. Jack, O.B.E. Dated 11th November, 1939.

Colonel S. G. S. Haughton, C.I.E., O.B.E., K.H.S. Dated 24th November, 1939.

Lieutenant-Colonel H. Williamson, O.B.E. Dated 23rd August, 1939.

Lieutenant-Colonel L. F. Brandenbourg. Dated 11th December, 1939.

## Note

#### GYNOMIN

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## Original Articles

### AORTIC STENOSIS\*

By GERARD KELLY, F.R.C.P.(I.)

MAJOR, I.M.S.

*Professor of Clinical Medicine, Medical College Hospitals, Calcutta*

THE fact that mitral stenosis, the unquestionable stigma of previous rheumatic infection, is a commonplace in many parts of India bespeaks the widespread presence amongst us of the seed, or hypothetical agent, that induces the rheumatic infection. In certain respects, India is the soil *par excellence* for the infectious agent: I refer to the sociologic factor, namely, the poverty of the masses in India and to the fact that India is the classical domain of deficiency diseases. The climatic factor too may be comprehensively assessed in the wide terrain of the Indian sub-continent with its unique range of climates. Finally, some parts of India have a seasonal abundance of streptococcal infections, such as tonsillitis, sore throats, acute sinusitis, and middle-ear disease which are often the precursors as well as important complications of our predominantly subacute rheumatism, which is not less serious than the rheumatic fever of England is dangerous. Accordingly, the rendition of satisfactory figures for our incidence of rheumatic heart disease would be much appreciated by those physicians abroad that are concerned with the rheumatic problem. If, however, we are to submit unimpeachable figures for our incidence of rheumatic heart disease and of other ætiological types of organic heart disease, we must adopt standard methods of classification and investigation and our clinical, electrocardiographic, radiological and pathological reports must be correspondingly accurate. I feel sure that if acceptable figures for the incidence of rheumatic heart disease were available to Homer J. Swift, he would hardly have stated at the First International Health Broadcast from New York in 1938 that 'Rheumatic heart disease rarely occurs among inhabitants of the tropics, unless they have contracted it elsewhere'. This paper on aortic stenosis and a previous one 'Some Notes on Clinical Heart Disease' (Kelly, 1939) are an attempt to indicate briefly some modern concepts of heart disease and methods of inquiry into it.

There are two main clinical groups of cases of aortic stenosis, the young and the elderly group. The fundamental pathology of both groups is essentially rheumatic. In young people aortic stenosis is the hall-mark of a severe rheumatic carditis in the past. In elderly men, that is to say in men over fifty years of age, aortic stenosis, according to Dry and Willius (1939) of the Mayo Clinic, is the outcome of progressive

calcification of aortic valves that have been slightly damaged by the rheumatic infection in early life. 'The time factor', remarked Dry and Willius, 'explains why calcification need not be a universal concomitant of healed rheumatic lesions, because those harbouring the more serious forms of the disease, especially when accompanied by mitral stenosis, are weeded out by death before such an event as calcification can occur, thus leaving the solitary aortic lesion, one that the heart tolerates far better than mitral stenosis, to continue for a long time without embarrassing the cardiac reserve'. 'The evidence derived from the study of this material (288 cases of calcareous disease of the aortic valve) has led us', stated Dry and Willius, 'to accept unequivocally rheumatic infection as the ætiological factor in calcareous disease of the aortic valve. Rheumatic infection which eventually culminates in calcareous stenosis of the aortic valve was originally a mild form of rheumatic carditis which has allowed both the mitral valve and the myocardium to escape with minimal or no damage'. 'Our material', they observed, 'was derived largely from the Middle Western States where, on the whole (as perhaps in India), mild and atypical forms of the disease may be anticipated'. 'The frequent absence of a rheumatic history in calcareous disease of the aortic valve clearly substantiates, in the opinion of Willius, his hypothesis that 'the original acute inflammatory episode was mild and perhaps so atypical that its significance could not be realized at the time'. He concludes that calcareous disease of the aortic valve 'is not rare' in the Middle West of America. 'It is possible', he remarks, 'that surveys in the regions where the disease (rheumatic infection) is more prevalent may show a relatively lower incidence of calcareous disease of the aortic valve'. The prevalence of rheumatic heart disease in Bengal may be approximately gauged from our hospital statistics given later in this paper. Until the distinctive features of calcific aortic stenosis are more widely known to the general practitioner its incidence cannot be fairly estimated.

#### *Rheumatic heart disease in hospital practice*

In the ten-year period, 1930 to 1939, there were 32,907 admissions (28,107 Indians and 4,800 Anglo-Indians) from all causes, to the medical wards of the Medical College Hospitals, Calcutta. Of these, 351 (310 Indians and 41 Anglo-Indians) were cases of rheumatic heart disease, as detailed below. Otherwise stated, one medical admission in every hundred was a rheumatic heart case. The prevalence however of cardiac rheumatism in Bengal is, in my opinion, somewhat less than our hospital figures suggest. Furthermore, the rheumatic infection in Bengal is more subacute than florid. 'Climate appears to be an important factor in the incidence both of the rheumatic infection and of the rheumatic type of heart disease. For example, in Boston at the Peter Bent Brigham Hospital

\* Being an elaboration of a paper read at the Calcutta Medical College Reunion, 1939.

the incidence of rheumatic fever in the years 1914 to 1923 was 1.85 per cent of all medical admissions, the clinical incidence of mitral stenosis was 3.89 per cent, and the incidence of mitral stenosis in the autopsy room was 4.68 per cent, while in New Orleans at the charity hospitals these percentages from 1916 to 1923 were 0.3, 0.08, and 0.23, respectively, and at Baltimore at the Johns Hopkins Hospital from 1914 to 1922, 0.73, 2.01, and 1.30, respectively' (White, 1937).

*Clinical diagnoses in the 351 cases of rheumatic heart disease treated at the Medical College Hospitals, Calcutta*

Mitral stenosis .. ..	120
Mitral incompetence .. ..	15
Double mitral .. ..	70
Mitral and aortic valve disease .. ..	25
Double aortic .. ..	4
Rheumatic carditis .. ..	107
Rheumatic aortic incompetence .. ..	4
Rheumatic pericarditis .. ..	6
	<hr/> 351 <hr/>

I have deliberately omitted a statement of the sex incidence, as in view of the purdah system the figures would necessarily be misleading. The criteria given in the *Nomenclature and Criteria for Diagnosis of Diseases of the Heart*, 1939, should be more generally employed in India for the classification and diagnosis of heart disease. Diagnostic inexactitudes, such as 'double mitral' and 'double aortic', should be abandoned: surely one of the lesions is predominant.

*Incidence of aortic stenosis—clinical group*

Calcereous disease of the aortic valve was diagnosed clinically in two of 1,832 cases of cardiovascular disease admitted to the Medical College Hospitals, Calcutta, from 1930 to 1939. McGinn and White (1934) of the Massachusetts General Hospital reported 113 cases of aortic stenosis (2.3 per cent) in 4,800 cardiac patients. Campbell (1937) observed that out of every six rheumatic cases three had aortic incompetence and mitral stenosis, the fourth had aortic stenosis as well, and the fifth and sixth were clinically without mitral disease, one having aortic incompetence alone and the other aortic stenosis and incompetence. A case of aortic stenosis and incompetence with mitral stenosis is described later in this paper.

*Incidence of aortic stenosis—post-mortem series*

McGinn and White (1934) reported 123 cases of aortic stenosis (1.8 per cent) in 6,800 autopsies of all types of disease. Of these 123 cases, 86 had calcareous changes in the aortic valve and 37 had aortic stenosis without calcareous changes: the majority of the former group were over 50 years of age, whereas the vast majority of the latter were under 50. The subjects of calcareous disease of the aortic valve are notoriously prone to sudden death. Hence calcific aortic heart disease is not infrequently encountered as a medico-legal cardiac case. Our

post-mortem material consists of a total of 1,995 cases of all types of disease autopsied in the period 1915 to 1937. I am grateful to Dr. M. N. De, lately Professor of Pathology, for the connected records, which suggest that aortic stenosis is practically non-existent in Bengal. Incidentally, if we are to develop a precise and scientific knowledge of heart disease in this country we must wherever possible supplement our clinical cardiology by pathological studies of our cardiovascular diseases and anomalies. Useful guidance may be had from the section entitled 'An Outline for the Pathological Diagnosis of Cardiovascular Diseases and Anomalies', in the New York Heart Association's standard work mentioned above. Seven international authorities on cardiovascular pathology are responsible for this section.

*Rheumatic aortic stenosis*

'As a rule, aortic stenosis is merely one element in rheumatic heart disease. It may be accompanied by aortic regurgitation, mitral defect, and myocardial and pericardial disease. In the pathogenesis of heart failure in such cases, aortic stenosis most often plays only a subordinate rôle. Actually, as a previously leaky valve narrows, the added work thrown on the left ventricle by the stenosis may no more than substitute for that spared the chamber by the diminution in regurgitation due to the constriction of the aortic aperture' (Fishberg, 1937). Aortic valvulitis, according to Horder, is particularly common in the endocarditis occurring during scarlet fever, a specific fever which I have never encountered in the tropics. Possibly school medical officers in certain parts of India may have some experience of it. Gallavardin's own rheumatic type of aortic stenosis in young subjects is probably congenital in origin rather than a subacute endocarditis of unknown ætiology. Miller advises us that aortic stenosis due to rheumatism is practically unknown in children. Signs of aortic stenosis in a child should arouse a suspicion of a congenital heart lesion or of malignant endocarditis.

*Calcific aortic stenosis*

Priority of description of calcific aortic stenosis belongs to Bonetus, who in his *Sepulchretum*, 1679, the early forerunner of Cabot's *Differential Diagnosis*, 1911, presented the case of the robust middle-aged Parisian tailor who dropped dead in the street and showed calcified stenosed aortic valves on autopsy. In 1931, Christian, the doyen of American cardiologists and the guru of Levine and others, wrote a significant paper on aortic stenosis with calcification. In this landmark in the study of aortic stenosis Christian not only concluded that calcific aortic stenosis was of rheumatic origin, but he also adumbrated the finding of calcification of aortic valves radiologically. In 1933, Sosman and Wosika described a fluoroscopic procedure whereby calcific aortic leaflets can be

visualized during life. Our interest in calcific aortic stenosis was immediately and enthusiastically revived.

#### *Evidence of the rheumatic origin of calcific aortic stenosis*

From a critical analysis of 200 cases of calcific aortic stenosis studied at necropsy, Clawson *et al.* (1938) decided that this lesion was invariably due to rheumatic infection. The following observations furnished the basis of their conclusion. The incidence of a rheumatic history and of stigmata of previous rheumatic infection in calcific aortic stenosis approximated that of other healed rheumatic deformities of the valve. The stigmata of previous rheumatic infection included deformities of the mitral or other valves, adherent pericardium, the presence of Aschoff nodes in the myocardium, a definite inflammatory reaction in 68 per cent calcified aortic cusps and aortic-valve vascularization in 95 per cent of cases. We know that blood vessels do not exist in human heart valves and that valve vascularization is secondary to rheumatic valvulitis (Gross and Friedberg, 1936, and Gross, 1937). 'That deposition of calcium', remarks Willius, 'should occur in a region of low vascularity, from which inflammatory products cannot be absorbed adequately, is one expression of the phenomenon of calcification in general'. 'The leaflets of the heart valves', continues Willius, 'satisfy this set of circumstances perfectly'. Cholesterol crystals, so commonly seen in atherosclerosis, were not seen by Clawson in any of the calcified aortic valves. The gross structure of the aortic valves in calcified valve deformity was, in Clawson's opinion, in all respects similar to the structure of the calcified mitral valves sometimes observed, and not at all characteristic of an atherosclerotic process. Atherosclerotic thickening of the aortic cusps is further negated, according to Clawson, by the remarkable smoothness of the aorta in the subjects of calcific stenosis. He suggests that the stenosed aortic valves, diseased from early life, buffer the systolic impact of the aorta and thus protect the ascending aorta. Willius' paper is on somewhat similar lines to that of Clawson's in the matter of evidence. They both stress the frequency of a rheumatic history and of stigmata of rheumatic infection, which they think is too great to be regarded merely as a casual and not a causative factor. Willius believes 'that rheumatic infection which culminates in calcareous disease of the aortic valve differs only in a quantitative manner and not in any qualitative manner, from other types of rheumatic carditis'. Other advocates of the rheumatic aetiology of calcific aortic stenosis are Christian (1931), McGinn and White (1934), Contratto and Levine (1937), and Boas (1935).

#### *Other views*

Friedberg and Solval (1939) do not preclude a non-rheumatic form of the disease. Margolis,

Zeilleesson and Barnes (1931) and others hold that in some cases the lesion is the result of a non-inflammatory degenerative process. Cabot's idea (1926) that calcareous disease of the aortic valve represents the healed stage of subacute bacterial endocarditis is, according to Willius, another intriguing but unsupported supposition. Libman suggests that congenitally bicuspid aortic valve may furnish the basis of some cases. Finally, it is to be remembered that syphilis is never a cause of aortic stenosis. About 30 cases of combined syphilitic aortitis and rheumatic disease of the heart have been reported up to date.

#### *Symptomatology*

'The only symptoms of aortic valve disease are the tendency to faintness, dizziness, or even syncope in patients with marked aortic stenosis' (White, 1937). We shall here confine ourselves to calcific aortic stenosis: the symptoms encountered in a case of aortic stenosis in young subjects are recounted later in this paper.

Calcific aortic stenosis is remarkably well borne by the left ventricle for many years. It is amenable to faultless compensation by the substitution of hypertrophy for dilatation at each stage, not only because of the inherent gradualness of the narrowing process but also because aortic and coronary sclerosis are likely to occur in inverse proportion to the degree of stenosis of the aortic valve. Eventually, the left ventricle yields behind the obstructed aortic orifice. The resultant effort-dyspnoea is often the earliest and may be the sole symptom for years. Cough due to chronic pulmonary congestion is commonly complained of and 'bronchitis' is often misdiagnosed, because of the patient's age and the absence of systemic oedema. Haemoptysis occasionally occurs. Later, paroxysmal dyspnoea may gravely distress the patient at night. The progress of heart failure in aortic stenosis is relentless. Finally, right-sided heart failure appears and death from cardiac failure, which is the commonest mode of termination of aortic stenosis, follows in about six months. The specific symptomatology of calcific stenosis, dizziness, syncope and angina pectoris, commonly occurs in the midst of these distressing symptoms of heart failure, and so may be displaced to the background of the clinical picture and pass unrecognized unless direct inquiry is made. The para-dyspnoeic angor of Gallavardin, or the sense of intense oppression in the chest sometimes amounting to actual pain associated with severe paroxysmal dyspnoea, must be clearly distinguished from true angina pectoris. 'Angina of decubitus' usually does not occur in aortic stenosis of calcific type. The not infrequent confusion of cardiac asthma with angina pectoris is ably discussed by Bedford (1939) in his excellent account of left ventricular failure in the Strickland Goodall Memorial Lecture.

*Angina pectoris*

About half the cases of calcific aortic stenosis exhibit angina pectoris. The mechanism of its production is myocardial ischaemia due to coronary insufficiency. For purposes of simplicity and clarity, I shall endeavour to summarize briefly the various explanations for this coronary insufficiency, ably advanced by Harrison (1939), Green (1936), Fishberg (1937), Contratto and Levine (1937) and Friedberg and Solval (1939).

When the aortic orifice is stenosed, thus obstructing the emptying of the left ventricle, the intraventricular pressure rises and the ejection velocity of the blood is greatly enhanced in order to maintain a given volume flow per unit of time. Now, the elevated intraventricular systolic pressure compresses the peripheral coronary vessels after the fashion of the blanching of a tightly-clenched fist and perhaps the accelerated blood flow past the coronary orifices produces suction of blood from the coronary vessels. Thus, coronary inadequacy may be present even at rest. Usually, however, this is more notable on exertion because the left ventricle, operating against the already extremely high intraventricular pressure, finds it difficult if not impossible further to augment the force of its contraction and the aortic pressure requisite for exertion. Increased heart size greatly intensifies such relative coronary insufficiency. The concentric hypertrophied heart of aortic stenosis is more appropriately described as 'heavy heart' than in terms of heart size. Verification of the theory of coronary insufficiency in these cases is frequently afforded by the coronary-thrombotic-like pattern of the T-wave and RST segments, which is in keeping with the clinical picture. The frequent presence of angina pectoris in 'pure' aortic stenosis, that is, without clinically evident aortic regurgitation, promptly dismisses aortic insufficiency as a causal factor of anginal pain in these cases. The occurrence of coronary vaso-constriction in calcific stenosis, with resultant coronary insufficiency, is purely hypothetical. In hypertensive arteriosclerotic heart disease subjects, the situation of coronary pain is not uncommonly atypical.

*Dizziness, fainting and syncope in calcific aortic stenosis*

These symptoms tend to occur in those aortic stenotics that suffer from angina pectoris as well. And like angina pectoris, attacks of faintness or downright syncope are complained of, mostly on exertion. Harrison attributes the syncopal attacks of calcific aortic stenosis to sudden diminution of the cardiac output, because of the aggravation by exercise of a pre-existing myocardial oxygen deficiency, with resultant cerebral anoxia. It may be extremely difficult to differentiate calcific aortic stenosis from coronary artery disease (arteriosclerotic heart disease). Both conditions are due to a common factor, namely, coronary ischaemia, with the

result that certain clinical and electrocardiographic features are common to both. Thus, they may both cause angina pectoris, cardiac failure and sudden death, and both may show conduction disturbances and T-wave changes electrocardiographically. In coronary arteriosclerotic subjects, however, syncope on effort fails to occur because, according to Harrison (1939), their myocardial anoxia is focal, whereas such syncope is a classical symptom of calcific aortic stenosis wherein myocardial anoxaemia is diffuse. A history of dizziness and syncope in an elderly man should therefore suggest the possibility of aortic stenosis rather than arteriosclerotic heart disease. The finding of an aortic systolic murmur and thrill would render the differentiation from coronary artery disease clear. In all doubtful cases the aortic valves should be carefully scrutinized fluoroscopically for evidence of calcification. Levine (1936) and others attribute the tendency of calcific aortics to faintness and syncope to hypersensitivity of the carotid sinus reflexes.

## DIAGNOSTIC CRITERIA

In 1934, McGinn and White advocated a considerable broadening of the previously rigid diagnostic criteria of aortic stenosis, which they concluded we were more often missing when it was present, than diagnosing when it was absent. In the opinion of Willius, the diagnostic criteria had not been recognized by the clinician until relatively recent years. Willius has closely studied aortic stenosis for many years and in such of his cases as failed to satisfy the old-time requirements necessary for a clinical diagnosis of aortic stenosis he sought radiological demonstration of calcification of the aortic leaflets. Truly 'the eye often misses what is not in the observer's mind but sees what it looks for'—Horder.

*Before 1934*

In his *Medical Notes*, Horder (1921) writes regarding a systolic murmur heard at the aortic base—'the first thing to say (to oneself) about a systolic bruit heard at the aortic base is that the case is probably not one of aortic stenosis. More likely causes of the bruit are . . . But if, in addition to the presence of a systolic aortic bruit, the following features are also made out during the examination—

- (1) good conduction of the bruit towards the right side of the neck;
  - (2) considerable hypertrophy of the left ventricle;
  - (3) systolic thrill in the second right interspace; and
  - (4) a small pulse—
- it may be said with confidence that the patient suffers from aortic stenosis. If to these findings were added—
- (5) diminution or absence of the aortic second sound; and



(6) an aortic diastolic murmur—  
 The most fastidious physician of previous decades would probably have registered his complete approval of Horder's excellent criteria. Incidentally it may be noted that five signs, namely, aortic systolic murmur, aortic diastolic murmur, diminished or absent aortic second sound, aortic systolic thrill, and calcification of the aortic valve on fluoroscopic examination in calcific stenosis, emanate directly from the deformed aortic cusps.

#### Since 1934

A fair sample of British and American requirements for the clinical diagnosis of aortic stenosis is given respectively by Campbell (1937) and by White (1937).

Concerning the diagnosis of aortic stenosis, Campbell states 'It is not so simple as that of aortic incompetence, although in cases of high-grade aortic stenosis it may at once be suggested by the feel of the pulse, both the slow rise and the sustained plateau being readily appreciated by the finger. A systolic murmur is often present as well as diastolic and may indicate nothing more than some roughening of the valves. Whenever there is a systolic murmur, a special search should be made for a systolic thrill and the rougher the murmur the more confidently may it be expected'.

'The combination of aortic stenosis and incompetence', he continues, 'is much commoner than pure aortic stenosis. It is sometimes said that only the expert should diagnose aortic stenosis in the absence of aortic incompetence, but the intention of this warning can be expressed better by the following statements. In the absence of aortic incompetence, stenosis should never be diagnosed unless there is a systolic thrill as well as a murmur, or the characteristic pulse of aortic stenosis or both.

In the presence of aortic incompetence, stenosis may be suspected even without a thrill if there is a very rough systolic murmur, especially if the pulse is less characteristic of aortic incompetence than would be expected from the loud diastolic murmur. The blood pressure should always be taken as a measure of the degree of stenosis and the pulse in both arms should be taken as a routine to detect the slighter cases of coarctation of the aorta'.

White's statement of the American attitude is as follows—'The triad of murmur, thrill and small pulse', he says, 'is the essential finding: the other findings are corroborative. It is not necessary to wait for an aortic systolic thrill or a plateau pulse to make a diagnosis of aortic stenosis: the diagnosis can be made on the systolic murmur alone in a patient without aortic dilatation or hypertension provided the murmur is loud and harsh. Accuracy of diagnosis has increased greatly in our hands since we have made this change in the diagnostic criteria of aortic stenosis'.

The essential criteria defined by Willis as diagnostic of calcareous stenosis of the aortic valve are as follows:—

(1) A loud rough systolic murmur over the base of the heart conducted into the vessels of the neck and in many instances over the præcordium.

(2) The second heart tone is absent or diminished in intensity.

(3) It is replaced by a soft blowing diastolic murmur where there is associated aortic regurgitation.

(4) A thrill is usually palpable over the upper part of the sternal region.

(5) Evidence of cardiac hypertrophy usually can be elicited.

(6) Radiological examination reveals the presence of deposits of calcium within the aortic cusps or annulus'.

#### BASAL SYSTOLIC MURMURS

Murmurs are obtrusive and impressive signs, and, if the physician is uncertain of their origins, he necessarily lacks self-assurance and diagnostic discrimination. While pulmonary systolic murmurs are commonly due to physiological factors and mildly pathological states, aortic systolic murmurs frequently own a definitely pathological basis of varying significance. The aorta is thicker, less elastic and much longer than the pulmonary artery, hence the aorta offers more resistance to distension and at the same time affords accommodation for a larger stroke volume than does the pulmonary artery. Therefore the increased cardiac output and heightened systolic force of the overactive heart (of excitement, anæmia, fever, neurocirculatory asthenia, thyrotoxicosis and early hypertension) are seldom sufficient to produce appreciable dilatation of the aorta. On the other hand, the resultant physiological dilatation of the soft, thin, easily dilatable short pulmonary artery in the same hyperkinetic circumstances is usually responsible for the pulmonary systolic murmur, the commonest of all heart murmurs, heard in Balfour's 'area of pulmonary romance'. (The right lung apex behind is another area of auscultatory romance.) Dilatation of the pulmonary artery and of its 'ring' would of course result in relative pulmonary incompetence: dilatation of the aorta and its 'ring' would likewise produce relative aortic incompetence.

#### Causes of aortic systolic murmur

##### I. Relative stenosis due to—

(1) Cardiac overaction, *e.g.*, in anæmia systolic murmurs are heard most frequently in the pulmonary area, next most commonly in the mitral area, the tricuspid area and the aortic area, in the order named.

(2) Simple dilatation of the aorta due to arteriosclerosis, chronic hypertension and syphilitic aortitis.

(3) Aneurysm usually of the ascending aorta.



II. Conditions favouring relative stenosis by producing kinking and so a tendency to proximal dilatation of the aorta, *e.g.*, high diaphragm, as in extreme obesity, pregnancy, ascites and other forms of abdominal distension.

III. Absolute stenosis due to—

(1) Monckeberg's sclerosis of the aortic valve without evident aortic dilatation, productive of slight aortic stenosis in some elderly people.

(2) Aortic stenosis due to rheumatic valvulitis or calcification of the valves (rheumatic and non-rheumatic calcific aortic valves).

(3) Congenital aortic stenosis productive of aortic dwarfism.

IV. Transmission of a systolic murmur from elsewhere, *e.g.*, pulmonary area, mid-sternum, lower sternum, apex.

### *The systolic murmur of aortic stenosis*

*Acoustic characters.*—The systolic murmur of aortic stenosis is characteristically loud and harsh. It may be rough, coarse, grating, croaking, vibratory, whistling, musical or even blowing. Rough murmurs bespeak stenosis, while rasping or tearing sounds often characterize the louder varieties of murmur associated with calcareous deposits on the valve, or marked stenosis. The murmur is apt to be very loud in recumbency. The loudness of the murmur is maintained until the grave heart failure of aortic stenosis supervenes, whereupon the murmur becomes less intense and may even disappear. The widespread transmission of very loud aortic systolic (stenotic) murmurs over the chest, back, vertex of head, sacrum and humeral condyles and their very occasional audibility, even at a distance from the patient, seems to support Cabot's view that 'the distance a murmur is transmitted is purely a function of its loudness'. Hence the 'loud and harsh aortic systolic murmur' postulated by White generally implies an obstructive stenotic murmur well conducted into the neck. Loud mitral stenotic murmurs are almost invariably confined closely to the patient's cardiac impulse because in diastole the apex is not firmly applied to the chest with the result that the vibrations are rapidly lost (Cowan and Ritchie, 1935). Thus mitral stenotic murmurs fail to endorse Cabot's theory of the transmission of murmurs.

### *Timing*

In aortic stenosis both the isometric and ejection phase of systole are prolonged. Sound records show that the isometric component of the first sound is clear of murmur provided that the disease process is limited to the semilunar valves. They also show that the murmur of aortic stenosis attains its maximum intensity in the phase of maximal ejection. Clinically, the loud and harsh murmur of aortic stenosis is early systolic in point of time, commonly masks the first sound and frequently extends throughout the whole of systole.

### *Punctum maximum*

This corresponds with that of the accompanying thrill, namely, the clinical aortic area. The murmur may, however, be best heard over the manubrium sterni or even to the left of the sternum. Rarely, the cardiac apex is the site of maximum intensity of the harsh stenotic murmur, in which case mitral regurgitation is simulated as it may be to a less extent when a loud aortic systolic murmur is heard all over the præcordium. In both instances, transmission of the murmur to the lung bases behind, significant of mitral regurgitation, is notably absent. Moreover, mitral regurgitant murmurs are not transmitted to the base of the heart, nor are they audible in the neck.

### *Selective propagation*

The transmission of the aortic systolic murmur of stenosis is characteristically widespread, because its vibrations are conveyed along the blood vessels in the direction of the blood current and also through the left ventricle, and because the louder it is the greater is its distance of transmission in accordance with Cabot's law, as stated above. Thus the murmur may be well conducted along the carotid and subclavian vessels into the neck and along the arms, it may be heard all over the front of the chest, and when it is heard in the back its point of maximum intensity precisely corresponds with the first point of contact of the aorta with the spine, namely, the fourth thoracic vertebra.

The transmission, however, of an aortic systolic murmur even into the neck is not pathognomonic of true stenosis: indeed, it is more frequently indicative of dilatation of the aorta with roughening of the intima. An interesting feature of aortic systolic murmurs is their tendency to 'tunnel', *i.e.*, 'to travel some distance underground and emerge with a change of quality'—Clifford Allbutt. 'The murmur of aortic stenosis', remarks Cabot, 'is often heard well at the apex and at the aortic area and faintly in the intervening space, probably owing to the interposition of the right ventricle'. Levine, who followed up many instances of such 'systolic murmurs—cause unknown', observed, 'as years went on a definite basal thrill would become palpable or calcification of the valve would be found on x-ray examination'. 'Dyspnoea or anginal pain', he adds, 'were frequent eventual developments in such patients'.

### THE THRILL

In the matter of physical signs in clinical medicine, not only is it vital to know them thoroughly and the precise technique of their elicitation but also to know when precisely to elicit them. Obviously, time for one thing does not permit a practitioner to perform all the tests in his repertoire every time he sees a new patient. With reference to aortic stenosis, Lewis aptly remarks that 'a harsh murmur is the hint to examine for thrill'. A thrill is the analogue of

the murmur, the conditions necessary for its production being more exaggerated as a rule. In fact, low-pitched murmurs are generally palpable as thrills. The essential requisite for thrill production is a sudden change in the calibre of the blood stream from narrow to wide. The most intense systolic thrills are those of aortic stenosis and pulmonary stenosis. Intensifying factors are a thin chest, closeness of the occurrence of the thrill to the palpating hand, and speed of blood flow. A common associate of calcific aortic stenosis is pulmonary emphysema, which causes recession of the heart from the chest wall. The force of the thrill varies with the intensity and pitch of the murmur. Hence a loud and harsh aortic systolic murmur is attended by a thrill, and if the murmur is a gentle one no thrill at all is felt. Thus, if an aortic systolic murmur is not fairly loud, generally it may be ignored. It is important to remember that when heart failure supervenes in aortic stenosis the thrill, like the murmur, becomes faint. The fainter thrills of aortic stenosis are often missed owing to faulty technique. For their detection it is necessary to employ light palpation with the patient sitting up and leaning forward, particularly with his breath held in expiration, whereby the sternum and adjacent ribs come into closer contact with the aorta, and the intervening lung border is retracted. One should carefully search for thrill in this fashion in the second right interspace, and over the upper and middle portions of the sternum. Occasionally the thrill may be felt at the cardiac apex, where it may very rarely be better appreciated than at the base. If in doubt about a thrill, the answer is 'thrill is absent'. Definite sustained purring vibrations must be felt before the observer can declare that thrill is present. An overacting heart throws the ribs, and more especially rigid ribs, into vibrations with the production of a 'pseudo-thrill', in which case, if one separates the fingers and places them in the intercostal spaces, the osseous vibrations will not be felt. The transmission of the aortic systolic thrill is similar to, but less widespread than, that of the corresponding murmur, and is likewise non-pathognomonic of aortic stenosis. A systolic thrill maximal in the aortic area is an indisputable sign of aortic stenosis, provided the other causes of thrill to the right of the upper end of the sternum, more especially those due to relative stenosis, *i.e.*, aortic dilatation and congenital heart disease, are excluded. The rarer causes of thrill to the right of the sternum are :—aneurysm of the ascending aorta or of the commencement of the aortic arch, aneurysm of the innominate or of the right subclavian artery, arterio-venous aneurysm (ascending aorta and superior vena cava) and compression of the aorta or its great branches by a mediastinal tumour or other factor. The thrill of arterio-venous aneurysm is continuous rather than simply systolic, especially over the site of perforation, *i.e.*, in the area about the aortic

cartilage. Kurtz has described the occurrence in the supersternal notch of 5 to 6 visible vibrations with each systole of the heart in cases of well-marked thrill due to rheumatic aortic stenosis.

#### *The aortic diastolic murmur*

An aortic diastolic murmur is the rule in rheumatic aortic stenosis, whereas it is an inconstant accompaniment of calcific aortic stenosis. The post-mortem evidence of calcific stenosis clearly suggests that leakage is inevitable, nevertheless clinical evidence of such leakage is not infrequently wanting, which reminds us that the murmur of mitral regurgitation is often conspicuously absent in fully developed mitral stenosis. In either case, the louder one murmur becomes the less loud is the other; that is to say, the greater the stenosis, the less the regurgitation. At all events a deliberate search should be made for a basal diastolic murmur in all cases of suspected aortic stenosis. A soft and distant aortic diastolic murmur is notoriously elusive. Such a murmur may be heard best after exercise with the patient standing or sitting and leaning a little forward, which manœuvre brings the aortic valves nearer the chest wall. We then listen attentively, employing a Bowle's chest-piece or direct auscultation with the naked ear, especially when the patient holds his breath in full expiration. The aortic diastolic murmur commences abruptly with, and may somewhat blur, the second sound; it quickly attains its maximal intensity during the first moment of diastole and is both less intense and less prolonged than its dominant partner, the loud, harsh and prolonged systolic murmur of aortic stenosis. In aortic stenosis, a maximal intensity and more clearly waterfall character of the diastolic murmur in the left third interspace close to the sternum, *i.e.*, approximately over the aortic valve itself, is highly significant of a rheumatic aetiology and of an undilated aorta. A loud aortic diastolic murmur should lead one to interpret a high intra-aortic pressure, the proof of a vigorous left ventricle, and a correspondingly less excessive leakage. 'The degree of aortic incompetence', Lewis reminds us, 'cannot be gauged from the loudness or length of the murmur'. A loud musical aortic diastolic murmur promptly excludes aortic stenosis in that such a murmur is usually due to retroversion or eversion of the right anterior aortic leaflet, produced by syphilitic involvement: a tear or rupture of an aortic valve is less commonly responsible for this loud musical murmur. The 'double aortic', beloved of students, is a finding of purely localizing value in that it implies nothing further than disease of the aortic valves. The confirmatory value of an aortic diastolic murmur in a case of suspected aortic stenosis is considerable in the absence of Corrigan's pulse, of alteration in the size and contour of the aorta and of evidence of syphilis.

### *The aortic second sound*

The careful determination of aortic second sound intensity is regarded by some observers as being of more importance in the diagnosis of aortic stenosis than the study of the pulse. The classical quartette of signs of aortic stenosis, however, is the loud, harsh aortic systolic murmur, the corresponding thrill, the diminished or absent aortic second sound and the plateau pulse. The aortic second sound and the pulse changes being usually difficult of interpretation are relegated to the third and fourth positions.

The second sound, which definitely precedes the opening of the mitral and tricuspid valves, gives acoustic expression to the vibrations set up in the semilunar valves at the moment of their closure and also on the wall of the artery and in the blood column itself (Orias and Braun-Menéndez, 1939). In classical aortic stenosis, the aortic second sound is weak or absent because the stiff and rigid valve segments are incapable of snapping together. Total absence of the aortic second sound documents gross stenosis. Elsewhere a second heart sound of subnormal intensity is easily audible. Even in well-marked aortic stenosis, the second sound is commonly heard at the aortic base and is due to the closure of the pulmonic cusps. Definite aortic stenosis can be present with a normal aortic second sound. The second sound, as heard at the aortic area, is the summation of the second sounds, originating in the aorta and in the pulmonary artery. Hence, when studying the aortic stenosis, it is advisable to auscultate the carotid artery also, where the aortic component of the second sound is isolated. Factors germane to consideration of aortic second sound intensity in aortic stenosis are the degree of stiffness of the aortic cusps, the presence or absence of an aortic diastolic murmur, the level of the systemic blood pressure, and the condition of the aorta. Extrinsic factors, such as obesity and emphysema, must of course never be overlooked in the evaluation of heart-sound intensity. A co-existent aortic diastolic murmur beginning abruptly in early diastole will somewhat blur the aortic second sound.

Lewis discusses accentuation of the aortic second sound in hypertension, wherein an accentuated aortic second sound is an expected, but by no means an invariable, finding. Obesity or emphysema may be responsible for its absence on occasions. Stiffness and enlargement of the aorta impart a slightly musical quality to the aortic second sound, hence an intoned or ringing aortic second sound suggests changes in the aorta rather than in the aortic cusps. Thus, in hypertension when the aortic second sound is reduplicated and ringing in quality (*bruit de tabourka*), the ringing quality is to be ascribed to sclerosis and calcification of the aorta and not to the hypertension. In aortic sclerosis without hypertension, the aortic second sound may be greatly accentuated and ringing, owing to the close

approximation of the sclerotic unfolded aorta to the chest wall. Otherwise stated, an aortic second sound with a characteristic snappy emphasis, comparable to the note of a small drum, is highly significant of aortic dilatation, especially if associated with normal blood pressure. As a general rule, therefore, state Norris and Landis (1933), if the aortic second sound is normal and more especially if it is loud and ringing in character, the systolic murmur heard at the aortic base originates in the aorta and is not due to rigid and diseased aortic valves. In calcific aortic stenosis the first part of the aorta is often remarkably free of atheromatous changes, owing to buffering by the calcific valves. Cabot's remark concerning the aortic second sound in certain cases of aortic stenosis is at least stimulating.

'Another strange fact is that even in a case with rigid and immovable valves the aortic second sound may not only be audible but may be actually accentuated and the systolic blood pressure high. How physiologists would account for this I do not know. So far as I see, it definitely attacks the theory, ordinarily held by physiologists, that the aortic second sound is due to the closure of the aortic valves and to this cause alone.'

We do not blame our physiologists for this apparent discrepancy.

### THE PULSE

The study of the pulse by palpation and tracings has greatly declined since the introduction of the baumanometer and the electrocardiograph. These instruments are of course infinitely more accurate in their assessment of pulse quality and rhythm: the rate being best obtained by auscultation of the heart. Nevertheless, it appears from Dudgeon's writing (1882) that the nineteenth-century physician armed with his 'loud-ticking gold chronometer' was at least more mysterious and consequently a greater oracle in his day.

'The physician of old made his diagnosis chiefly by observation of the pulse and tongue. But as the tongue could be rapidly inspected, and anyone could judge of its foulness or cleanness as well as himself, he concentrated his attention mainly on the pulse, in the feeling of which there was always scope for affecting the possession of peculiar skill and insight. To the uninitiated, who regarded the doctor as a depository of occult knowledge, and who received his dicta as though they were oracles, there was something very imposing in his method of pulse palpation. The fingers of the right hand daintily grasping the patient's wrist, while the doctor's eyes are riveted on the loud-ticking gold chronometer he held in his left hand, his head gravely nodding the while synchronously with the arterial pulsation—all this formed a picture calculated to inspire beholders with reverence and awe.'

'The outstanding diagnostic sign of aortic stenosis is a *small pulse*, rising slowly to a delayed summit . . . Aortic stenosis should never be diagnosed without this sign'—Lewis. The characteristically slow, small, retarded pulse (*pulsus rarus, parvus, tardus*) is the peripheral expression of 'pure' aortic stenosis of high-grade severity. Its wave conveys to the finger the impression of a gradual rise to a summit which

is unduly prolonged in the form of a plateau. The sustained plateau is best appreciated by palpation with the approximate fingers simultaneously, when the pulse wave will be felt to take time to pass the palpating fingers, like a crowd going through a door. Left ventricular hypertrophy may compensate for the stenosis, and so the size of the pulse may be approximately normal. Whereas the plateau pulse feels full between the beats, Corrigan's pulse feels empty. The slow rise bespeaks obstruction to the ejection of blood from the left ventricle into the aorta due to the absolute narrowing of the valvular orifice. Anacrotism, or the presence of an additional wave on the upstroke of the pulse, marks the transition from a rapid to a slower ejection by the left ventricle.

The causal factors of this sudden change of ventricular tactics are not yet precisely known. The valvular obstruction and perhaps coincident arteriosclerosis are probably responsible. The anacrotic pulse is more diagnostic of aortic stenosis than the *pulsus bisferiens*, or the double pulse beat, but it is not pathognomonic of stenosis in that it is also observed in conditions of obstruction distal to the aortic valve, e.g., aortic aneurysm, compression of the radial artery by a tumour proximal to the site of palpation, severe arteriosclerosis, etc. Both the anacrotic pulse and the *pulsus bisferiens* are usually more evident in pulse tracings than they are to the palpating finger. Another feature of the classical pulse of aortic stenosis is delay, i.e., increase of the normal interval between the cardiac apex and the radial pulse to perhaps one-fifth of a second, which increase is most evident on simultaneous auscultation of the heart and palpation of the radial pulse. This retardation of the pulse is connoted by *tardus*. The heart rate in aortic stenosis is often remarkably slow, even 50 to 60 beats per minute, in the absence of heart block and digitalization.

Harrison (1939) suggests that the carotid sinus is reflexly concerned in the prolongation of systole common in these cases and that the duration of diastole is correspondingly lengthened, which conditions tend to delay the onset of the next heart beat. Levine remarks—'the slow heart rate may possibly be due to the same factor that makes the patient subject to syncope, or may in some way be related to the vagus apparatus'. However it may be, the bradycardia of aortic stenosis maintains a satisfactory diastolic pressure, thus obviating anginal seizures, which tend to occur with higher heart rates. Most patients with congestive failure exhibit tachycardia and may have arrhythmias. In aortic stenosis, however, the heart rate, even in advanced congestive failure, may be under 70 or 60 in the absence of heart block and digitalis therapy. The rhythm, moreover, is generally regular. Such a congestive failure, or for that matter any congestive failure of obscure aetiology, should always remind one of the possibility of calcific aortic stenosis. The

three characteristic pulses of valvular disease of the heart are Corrigan's pulse, significant but by no means pathognomonic of aortic regurgitation, the plateau pulse of aortic stenosis, and the small pulse with firmness found in mitral stenosis. Corrigan's pulse is a popular finding not only in aortic regurgitation but also in conditions of peripheral vaso-dilatation and high pulse pressure, e.g., Graves described it in hyperthyroidism, it may be a conspicuous feature of certain anæmias, it is a common feature of neurocirculatory asthenia and during fevers: it may be observed in some cases of hypertension.

For the occurrence of Corrigan's pulse in aortic regurgitation, the leak must be appreciable and the left ventricle must be fairly powerful. Hence in cases of slight leakage, widely-gaping aortic orifice, or of left ventricular failure, Corrigan's pulse is absent or indeterminate. Its form is the antithesis of the plateau pulse and both aortic stenosis and mitral stenosis definitely modify it. The classical plateau pulse is not a feature of the majority of the cases of aortic stenosis. The young rheumatic group, for example, is characteristically polyvalvular and so the pulse is the resultant of aortic stenosis, aortic incompetence, and perhaps of mitral stenosis. Aortic stenosis tends to lessen both the rise in systolic pressure and the fall in diastolic pressure due to aortic regurgitation. Mitral stenosis modifies the signs of aortic regurgitation in much the same way. In the calcific group, in addition to the usual presence of aortic leakage, one not infrequently finds a complicating hypertension, the classical pulse of which is described as '*magnus, durus, tardus*'—large, hard and slow.

Other associates of the elderly group are arteriosclerosis and renal disease. Both groups may exhibit a superimposed neurocirculatory asthenia. Obviously the pulse, like the aortic second sound, is often difficult of correct interpretation. 'Indeed I have in two cases observed a well-marked "Corrigan" pulse in life, and been confronted post mortem with a narrowed, rigid aortic valve!' Cabot's perplexity is eloquent.

#### *The cardiac impulse*

The characteristic cardiac impulse of gross aortic stenosis is large, rises gradually, is overlong sustained and leads to a slow, deliberate and well-defined displacement of the thoracic wall, downwards and slightly outwards. Briefly, it displays increased force and a slow and deliberate out-thrust. 'The out-thrust of the apex beat may be even slower and longer than in the case of hypertrophy—"slow heave", which is sustained'—Price (1937). It is reminiscent of the slow steady heave of a bullock starting to drag a heavy bullock cart. Libman suggests that the contrast between the slow heaving cardiac impulse and the absence of retromanubrial pulsation may afford a clue to the recognition of

aortic stenosis. Broadbent describes the cardiac impulse of aortic stenosis as 'a well-defined and deliberate out-thrust of no great violence'. The distinctive impulse should be compared with the delayed flat-topped pulse wave of small or average volume. When heart failure supervenes, the slow heaving impulse of aortic stenosis becomes more diffuse. The combination of a feeble first heart sound and a heaving impulse is as significant of cardiac failure as it is striking to the observer.

### *The first heart sound*

Four factors—muscular, valvular, vascular and auricular—contribute vibrations to the first heart sound (Orías and Braun-Menéndez, 1939). For the normal production of the first heart sound mitral and tricuspid valve closure must be prompt and efficient, and strong ventricular muscle must produce a sudden well-marked pre-sphygmie tension preceding the outflow of blood. Two groups of ventricular vibrations are essential for the formation of the first heart sound: the first group, produced by the sudden contraction of the ventricle, is known as the isometric component, and the second group, produced by the opening of the semilunar valves, is called the ejection component. Furthermore, the intensity of the first heart sound varies directly with the rate of rise of intraventricular pressure during systole and does not depend on cardiac output (Wright, 1936). The degree of tension to which the mitral and tricuspid valves are subjected at the beginning of systole, is the other principal factor determining the intensity of the first heart sound. Recently, Stead *et al.* (1939) concluded that in normal hearts the position of the auriculo-ventricular valves at the beginning of ventricular contraction is the primary factor in determining the character of the first heart sound. Variations in the P-R interval within normal limits, they observed, may produce striking alterations in the first heart-sound intensity. In aortic stenosis there is obstruction to the outflow of blood and consequently a super-normal intraventricular systolic pressure with prolongation of both the isometric and ejection phases of systole. Hence the first sound at the apex in aortic stenosis is typically booming, *i.e.*, prolonged, low-pitched and resonant, signifying concentric left ventricular hypertrophy. At the aortic base the first sound is commonly masked from its commencement by the loud harsh aortic systolic murmur. Marked prolongation of the first sound in aortic stenosis may be the whisper of an approaching gallop rhythm, indicative of left ventricular failure. Presystolic gallop rhythm is 'the cry of the heart for help'. Not rarely, however, gallop rhythm suggests the presence of bundle branch block, which is sometimes a helpful diagnostic feature of calcific aortic stenosis. The Austin-Flint murmur is interpreted by some as a presystolic gallop rhythm (Laubry and Pezzi, 1926).

### *Blood-pressure readings*

Classical aortic stenosis exhibits a low systolic and relatively high diastolic pressure, *e.g.*, a frequent reading is 110/90. The resultant is a small pulse pressure. We have already referred to the influence exerted by the stenosis on the commonly associated aortic leakage, which influence is less notable in rheumatic stenosis. Reference was also made to the fact that the essential hypertension not infrequently complicates the calcific group. 'To some extent', remarks Willius, 'the height of the blood pressure bears an indirect relationship to the degree of stenosis, although even in extreme degrees of stenosis severe hypertension and all its peripheral associates may occur'.

Speaking of blood-pressure readings, I might mention in passing that John Parkinson constantly insisted that 'there was no such disease as low blood pressure'. 'Usually', said Stroud (1939), 'individuals with low blood pressure can be patted on the back and told that God has been very kind to them. They do not accomplish quite as much as the high pressure individuals, but they are wonderful from the standpoint of the physician. They never feel quite right, they are always coming back to them and they live for ever'. The fat type of Bengalee gentleman is rather more concerned with high blood pressure: indeed he not infrequently displays Musser's syndrome, namely, obesity, hypertension and glycosuria. 'In old age, when the aorta is sclerosed, the diastolic pressure may be relatively low, and such a reading as 200/90 obtained. These readings may not be indicative of true hypertension'—East and Bain (1936).

### *Electrocardiographic changes*

The electrocardiogram in aortic stenosis expectedly reflects left ventricular strain. This is evidenced electrocardiographically by (1) left axis deviation and by (2) changes in the T-wave in lead I or in leads I and II. Disturbances of rhythm may be present also.

### *Axis deviation*

Left axis deviation is the common finding. A large excursion of R in lead II is not uncommon. The differential effect in the two ventricles caused by combined aortic and mitral lesions may be shown by left axis deviation, right axis deviation, or no preponderance. Auricular fibrillation is usually associated either with right axis deviation or with no preponderance of either ventricles. This, in the opinion of Willius, suggests that as long as the left ventricle carries the major strain, the auricles are far less likely to fibrillate than when the reverse is true.

### *T-wave changes*

Inversion of T-wave in leads I and II is due either to factors which act directly upon the muscle or to a change in sequence of invasion as in bundle branch block. In the latter case, the



T-wave changes are associated with QRS changes. In aortic stenosis, with the development of left axis deviation, the T-wave in lead I becomes flattened and finally inverted. Such inversion of the T-wave in lead I may be indicative of the beginning of a not uncommon conduction disturbance in calcific aortic stenosis. I refer to left bundle branch block, which may sometimes be explained in these cases by an extension of the calcific process from the aortic valve to the bundle branch. Inversion of T in leads I and II is common in great enlargements of the left ventricle, when it may signify a relative myocardial ischaemia, due more to the enormous muscle mass increasing the territory of the coronary circuit than to the decrease of the coronary blood supply by the lowered cardiac output of aortic stenosis. T-wave changes in leads II and III suggest the presence of a complicating factor, such as mitral stenosis or pulmonary arteriolar sclerosis, in both of which cases right axis deviation will be in evidence. Otherwise digitalization or coronary infarction may provide the explanation. T-wave changes in all three leads suggest a complicating mitral stenosis or some other less easily discernible factor. A diphasic T-wave in lead I or II of the  $\mp$  type has the same significance as inversion of the T-wave. T-wave inversion tends to lengthen the relative duration of systole. It is much less ominous in aortic stenosis than when associated with grave myocardial involvement.

### Diagnosis

The clinical diagnosis of aortic stenosis should be primarily founded upon the secure basis of a fairly loud aortic systolic murmur and its corresponding thrill, as described above. If a diagnosis of aortic stenosis is going to be made by physical signs at all, the murmur and thrill are fundamental signs without which diagnosis will generally proceed uncertainly, until radiological and electrocardiographic aid are invoked. In the *mofussil* such instrumental assistance is rarely available. Amongst the foremost contributors to our present knowledge of aortic stenosis are Christian and his former pupil Levine.

'Without the thrill in addition to the murmur, it is unsafe to make a diagnosis of aortic stenosis. If diagnosis is limited to the cases which present both the thrill and the murmur, the percentage of correct diagnosis will be high. On the other hand, a few cases will be missed for we do see aortic stenosis in which no thrill is produced or even without a murmur. Sometimes this failure to feel a thrill and hear a murmur results in examining the patient only in the late stages of the disease when decompensation is marked' (Christian, 1935).

'The clinical diagnosis of aortic stenosis will in most cases depend on finding a systolic thrill at the base of the heart' (Levine, 1936).

The next step is a diligent search for an aortic diastolic murmur. Its discovery will aid a focal diagnosis of aortic valve disease, and will further suggest that the loud aortic systolic murmur bespeaks absolute stenosis. The intensity of the aortic second sound should then be carefully

estimated in the manner described. Its decrement confirms a diagnosis of absolute stenosis. In the absence of a typical plateau pulse, the observer should at least satisfy himself that the pulse is not an unmodified Corrigan pulse. The first heart sound, the cardiac impulse, and the neck and radial pulses should be studied and contrasted the one with the other. The variability of the blood pressure and the connected factors are briefly discussed above. In emphysematous and obese calcific aortic subjects especially, x-ray examination is the only precise method of determining heart size, especially left ventricular enlargement and local or general aortic dilatation: the technique of visualization of the calcified valves is described by Sosman and Wosika (1933); left auricular enlargement finally confirms any clinical signs of mitral stenosis. The electrocardiographic findings in the calcific group have been recorded. Those in the rheumatic group likewise add to the completeness of the clinical picture, e.g., the type of preponderance or neutralization, the severity of the cardiac lesions, the progression of carditis, and so forth.

A pure rheumatic aetiology is indicated by the youth of the patient, and a previous history of rheumatism or the presence of mitral stenosis clinically or enlarged left auricle radiologically and the electrocardiographic picture. The calcific group, on the other hand, is over fifty, has a distinctive symptomatology, exhibits conduction disturbances electrocardiographically, and perhaps calcified valves on fluoroscopy. We have already referred, under 'syncope', to the differentiation of calcific aortic stenosis from arteriosclerotic heart disease or coronary artery disease.

Sosman advises us to suspect the possibility of combined rheumatic aortic stenosis and syphilitic aortitis in cases of obscure and bizarre cardiovascular disease in which there is a history of previous rheumatic fever and clinical evidence of syphilis. Clinically, it is usually impossible to establish the diagnosis of such a combination, which occurs more frequently in localities with a higher incidence of syphilitic aortitis. There is, however, no clear evidence as yet that one predisposes the heart to a subsequent infection by the other.

### PROGNOSIS

'Rheumatic aortic stenosis', Campbell (1937) tells us, 'is of serious significance in the young subject, its gravity being related to the size of the heart: but if all signs and symptoms are favourable, aortic stenosis is compatible with a good prognosis'.

The subjects of calcific aortic stenosis, and more especially those with angina pectoris, dizziness, syncope, conduction disturbances and marked cardiac enlargement, exhibit a distinct liability to sudden death, sometimes in the midst of their usual health, that is, before heart failure



has finally supervened. In such cases the occurrence of sudden death may be very occasionally explained on a mechanical basis, namely, by locking of the valve by an unusually forceful diastolic recoil thrust, or by thrombotic occlusion of the stenotic aortic orifice, as may happen in very rare cases of mitral stenosis with a ball thrombus in the left auricle. In some cases of calcific stenosis the cardio-inhibitory action of a hypertensive carotid sinus may be productive of cardiac standstill and sudden death. More usual explanations of sudden death in calcareous disease of the aortic valve are ventricular fibrillation, the result of oxygen deficiency due to severe myocardial ischaemia, which may also produce high-grade heart block with consequent cerebral anaemia or cardiac standstill. Acute coronary occlusion caused one death in Willis's series; another case of his exhibited all the features of coronary thrombosis, including the classical electrocardiographic pattern, yet necropsy revealed no evidence of any such vascular accident. Incidentally, a single attack of acute cor pulmonale may produce a remarkable clinical and electrocardiographic likeness of acute coronary disaster without morphological evidence of coronary insufficiency. The physician in charge of a puerperal case, for example, may invite one to see an acute pulmonary embolism whose clinical features, namely, shock, sudden air hunger, sense of impending dissolution and sub-sternal oppressive pain, have not unreasonably raised a suspicion of coronary thrombosis. As a matter of fact, when the pulmonary artery or its main branches are suddenly obstructed, the lesion is in effect a coronary one, in that the increased tension in the right ventricle diminishes the blood flow through the right coronary artery with consequent coronary insufficiency, myocardial ischaemia, and a preponderantly right coronary pattern of the electrocardiogram. Coronary thrombosis itself implies a progressive degenerative arteriosclerotic process with eventually initial haemorrhage, thrombosis, and occlusion of a coronary vessel, in this order. Lest the gravity of calcific aortic stenosis has been rather over-emphasized, we shall cite the cases of the Latin professor and college dean, who had evident valvular heart disease for at least 25 years. In his sixty-third year the professor consulted White (1932), who found marked calcific aortic stenosis and considerable cardiac enlargement but no congestive failure. 'During the following one and a half years he did very well' remarked White, until one summer 'he was fatigued by college commencement exercises and the hot weather, and then motored off into the country nearly 200 miles in one day'. That night the professor not undeservedly had an attack of pulmonary oedema. He died a few months later. 'The first qualification of a physician is hopefulness'—James Little. And at the bedside of a heart case a great deal too much optimism is, to quote Lindsay, a venial error compared with a little too much pessimism.

'As a rule', remarks Levy, 'even those, who stoutly assert that they "want to know everything", prefer to hear a word of encouragement'. If you feel inclined to flourish the sword of Damocles, you might advisedly recall the observation of Wilks, that 'the sleeping accommodation of all the London hotels would be insufficient to put up the individuals walking about the city who had at some time or another been condemned to death by the medical profession'.

#### MYOCARDOSIS

Hyman and Parsonnet in introducing their *Failing Heart of Middle Life* (1932) informed us that

'The intense publicity given (heart disease) by every agency has swept into many a physician's consulting room individuals who had never before sought medical advice. Probably no phase of health propaganda has excited more interest among the laity than the problem of heart disease. Presented by the startling fact that heart disease leads all other causes of death, notwithstanding the tremendous publicity given to cancer and tuberculosis, many persons have besieged their doctors to examine them and to allay their fears of sudden death from heart failure. With the daily press constantly relating the sudden demise of some prominent citizen from causes said to be heart disease, the problem is more sharply brought to the attention of newspaper readers approaching middle life.'

The writers tactfully met this situation by 'an attempt to portray for the reader a more or less tangible and subtle picture of the failing heart before there are demonstrable objective signs of frank cardiovascular pathology'—the so-called myocardosis syndrome. From the outset we have discountenanced their equivocal term 'myocardosis', convinced as we are in the truth of Stroud's remark that a great many of these 'failing hearts of middle life' are merely introspective, apprehensive individuals who are afraid of heart disease but have nothing wrong with their cardiovascular systems any more than God expects them to have as they grow older.

Willis (1931) found abnormal electrocardiograms in 55 per cent of 700 people over the age of 74 years. Everybody naturally is afraid of heart disease and in America its danger and fatalities have been disastrously over-emphasized by every agency, for example by pamphlets such as 'How is your heart', by posters entitled, 'Your heart is a pump, take care of it', complete with a picture of a pump and a skeleton working at the handle, by broadcasts on heart disease, by overcautious physicians, and by divers other means. In his presidential address to the American Heart Association in 1939, Dr. Stroud admitted that all this heart disease propaganda, originally designed to prevent heart disease, has been a source of worry to him for many years in view of the very many imaginary-heart-disease sufferers it had produced. Dr. Stroud then appealed to the profession in America 'to dispel some of the fear in the mind of the average man concerning cardiovascular disease'. He condemned the publicity methods mentioned above and expressed his agreement

with the sound British attitude by his remark that—'the English certainly feel that we are taking grave chances in bringing too much of this subject before the public, which is not well enough trained to really understand what it is all about'. Certainly, learned addresses to public audiences on 'sudden death' and on what the Irishman calls 'coroner's thrombosis' are not in the public interest. 'Certainly', continued Dr. Stroud, 'we have enough to be afraid of nowadays—social security, wars in Europe, many, many things. If we give our patients a philosophy of life and hope and faith, I believe that we are helping them more than if we make them fearful'. Problems in regard to sudden death and the Insurance and Workmen's Compensation Acts increasingly worry the American lawyer to-day. But he is not complaining. All these considerations decided us to exclude 'myocardosis' from our heart diagnoses in India; 'myocardosis' and 'silent heart disease' are much too subtle for the general public.

#### REMARKS

Clinical features are stressed throughout this paper because the fundamental basis of a sound knowledge of heart disease is necessarily clinical. Furthermore, substitution procedures such as electrocardiography are not really available to the rural practitioner who is still compelled to rely entirely upon his previous clinical training, stethoscope, blood-pressure instrument and watch for his cardiac diagnosis. The relative value of the different procedures employed in the investigation of a heart case is clearly stated by White (1937) in his *Heart Disease*. 'Electrocardiography', he said, 'ranks third in value after history taking and physical examination: cardiovascular radiography ranks fourth'. 'The electrocardiograph', he insisted, 'does not take the place of such other methods of examination as history taking, percussion, auscultation, and radiography'.

Obviously no cardiologist would attempt to exalt electrocardiography by depreciating clinical investigation. On the contrary, *Diseases of the Heart* by Lewis (1937a), the foremost authority on electrocardiography, is the finest appreciation of clinical heart disease I know. We briefly discussed cardiac symptoms and signs in a previous paper (Kelly, 1939). The doubtful symptoms and signs displayed by obese and emphysematous subjects had been discussed already in some detail in *Recent Advances in Cardiology* (East and Bain, 1936) and x-ray examination and electrocardiograms advised. John Parkinson, however, remarks that 'when a patient complains of pain about the sternum when he walks, the diagnosis of a healthy heart is out of the question'. The most innocent undergraduate knows that an isolated symptom or sign rarely makes a diagnosis, any more than that 'one swallow makes a summer'. 'Experience teaches', says Lewis, 'that to place reliance

upon a single sign is precarious. Compare this sign with that, and confident recognition of the patient's state grows as these signs group themselves together to form a harmonious picture'. We used neurocirculatory asthenia to illustrate this linkage of symptoms and signs to form a clinical picture, which incidentally had not heretofore been sufficiently emphasized to the general practitioner in India. 'The modern routine examination of heart cases', we said, 'includes clinical, electrocardiographic and radiological examination'. The case reported demonstrates how the latter procedures corroborate and supplement the clinical findings. The routine investigation of a heart case in the outpatients' department of the National Heart Hospital, London, is as follows: The technician takes the electrocardiographic tracings of the case before the physician's arrival. The tracings are then taken over by the sister in charge, who places them in their rack in the physician's room. The physician personally takes the history, performs the physical examination and makes a clinical diagnosis in each case. The appropriate electrocardiogram is now picked out of the rack and handed to the physician, who interprets it in conjunction with the clinical picture. When all the cases are thus disposed of, the patients are taken to the x-ray department. The physician personally screens each case and outlines on tracing paper the radiological configuration of any case of special interest, correlating all the while the clinical, electrocardiographic and radiological findings. The technical assistant in most electrocardiographic departments can 'rattle off' electrocardiographic findings, e.g., arrhythmias, on sight. They fail, however, to attain the status of the physician in that they cannot correlate the electrocardiographic with the clinical findings. The physician in charge of a case should not regard a mere statement of electrocardiographic findings, such as the technical assistant may provide, as the electrocardiographic interpretation of his case.

Clearly, every physician should interpret the electrocardiographic findings of his own cases in the light of his clinical knowledge of them. To this end physicians should acquaint themselves with the essentials of clinical electrocardiography. These are to be found in *Clinical Electrocardiography* (1937) by Lewis, who tells us that this handbook of only 120 pages is 'intended to serve as an introduction to students of electrocardiography and as a guide to practitioners and hospital physicians in understanding curves that may be taken by others from patients in their charge'. Lewis deals in his excellent way with disturbances of the cardiac mechanism. There is a great and rapidly increasing demand by the American practitioner of medicine who does not intend to specialize in cardiology for handbooks designed to give him a grounding in electrocardiography. *Essentials of Electrocardiography* by Ashman and Hull (1937) is such a handbook. These writers state

that they 'have removed the emphasis from disturbances of the cardiac mechanism and have placed it where it belongs, namely, upon the abnormalities, which reveal or suggest the existence of myocardial disease'.

The rough summation of an electrocardiogram consists in the simple addition of the observed deviations from the normal. Leads I and II are particularly scrutinized for abnormalities, which are usually less significant if confined to lead III. One minor electrocardiographic abnormality may be disregarded. The addition of several inconclusive deviations equals heart disease just as does the sum of several inconclusive clinical findings. Chest leads are of much value and should be requested more frequently, especially lead IV, F.

In the not too distant future the lag-screen belt electrocardiogram will be a commonplace adjunct in the bedside diagnosis of heart cases in India, as it already is in America. This enables the physician, who can interpret electrocardiograms, to see precisely what is going on in the heart. In fact, some physicians have already complained that the machine is not infrequently a source of embarrassment, in that it compels a decision on the spot as to treatment, whereas formerly the physician could look the matter up quietly while the film was being developed. Large numbers of army recruits with alleged heart disease could be quickly and finally disposed of by the lag-screen method of Asher.

'Finally', concluded White, 'it must be realized that the electrocardiogram may be perfectly normal even in the presence of serious heart disease'. The truth of the latter remark is specially emphasized by Lewis (1937)—'It is to be recognized', he said, 'that a thrombosis may happen in the coronary arterial system without appreciable change being displayed then or subsequently in the electrocardiogram'. Thus there are silent areas in the myocardium as well as in the frontal lobe. Nevertheless, I do not propose to disturb the profession or the public by over-stressing silent heart disease. The phrase is too sinister, too suggestive of sudden death, especially to the middle-aged man, who not unreasonably derives much consolation from the thought that his doctor can 'spot' something wrong with his heart by some means or other, and thereby forestall what is dramatically described as a myocardial catastrophe. The third-year medical student is aware of the dangers of dual failure in diphtheria, and the general practitioners I have met never fail to suspect circulatory failure in a case of diphtheria whatever the signs. The remarks of Boyle *et al.* (1939) concerning this circulatory failure are not uninteresting. 'Surprisingly', they said, 'death from this cause is frequently not entirely explained by the pathologic changes in the heart. The frequent paucity, or even absence of cardiac lesions, contrasted with the dramatic collapse in

diphtheria, has led some authors to look elsewhere for the cause of death, or to hypothesize a functional alteration of the myocardium'. Paul White's attitude towards electrocardiography is well balanced. 'This method of study', he said, 'should be viewed modestly as helpful and supplementary but not accorded too great importance'.

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#### Case report

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His family history was negative. He had malaria and eczema in childhood. At the age of ten he was confined to bed for several weeks on account of a moderately severe grade of fever, attended by sore throat and flitting arthritis. For a whole year thereafter he had an evening temperature and experienced palpitation and dyspnoea whenever he tried to get about. In fact, ever since he had that long-drawn-out fever fourteen years ago he has constantly noticed that moderate exertion brings on some degree of palpitation together with a less degree of dyspnoea. From time to time in the past five years a feeling of mild general weakness comes over him. Lately, he has been having night starts and bad dreams and also feelings of faintness. To-day he had an attack of actual syncope.

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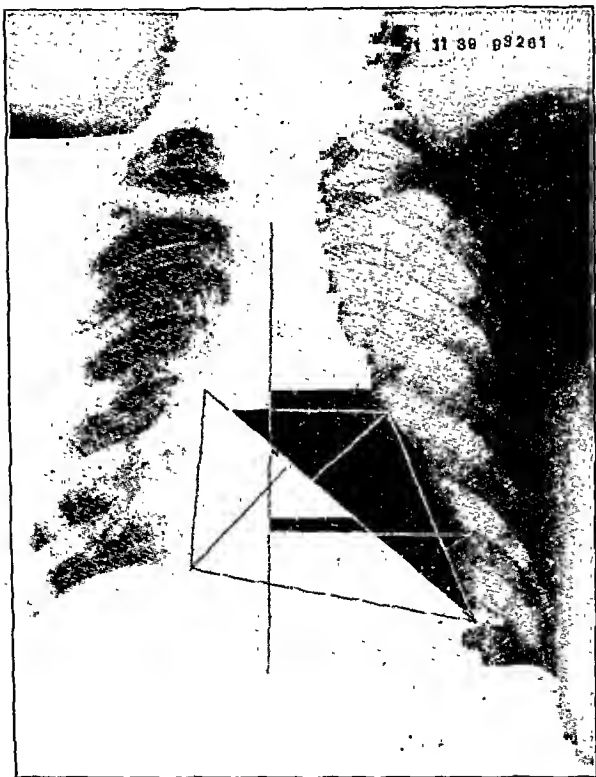
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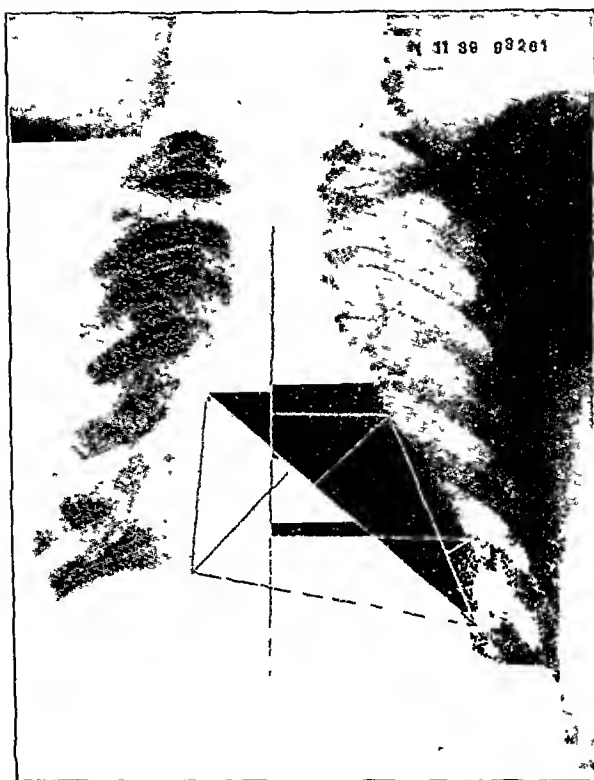
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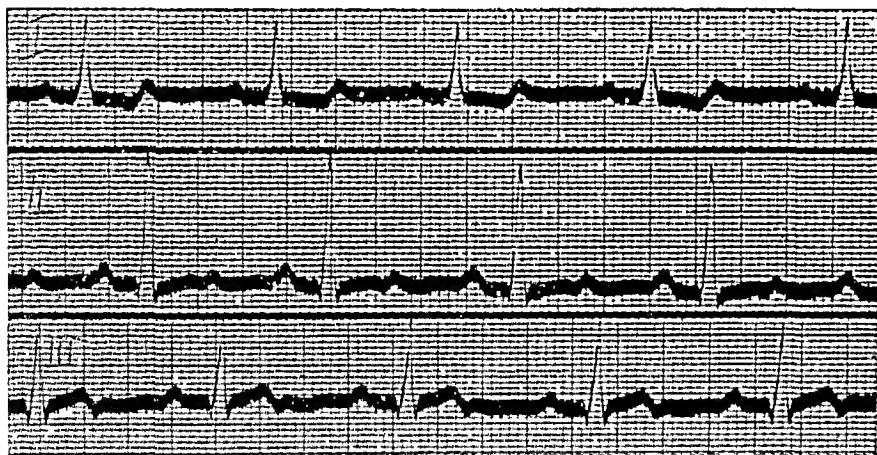
*Comment.*—This patient is evidently introspective and apprehensive. His reflexes and emotional responses are brisk. There is nothing, however, that shakes the general morale of any individual more than the occurrence of attacks of faintness or actual syncope. The underlying mechanism responsible for syncope in young people is usually neurogenic (vaso-vagal syncope) and in them syncope is generally benign. Paroxysmal tachycardia is an occasional cardiogenic cause of syncope in young persons. Aortic valvular disease is the only form of valvular disease causing syncope. In this case syncope owns a neurogenic mechanism. If, on the other hand, the patient were an elderly man, we would first exclude a cardiogenic origin such as Adams-Stokes' syndrome, certain tachycardias, *e.g.*, fibrillation and flutter, myocardial insult, *i.e.*, coronary thrombosis, and calcific aortic stenosis. We would also remember that cerebral arteriosclerosis might be a factor in the case. And in elderly men with arteriosclerosis or hypertension, we might occasionally diagnose carotid sinus syncope of which there are two

these were the cases that Gowers relegated to the borderland between epilepsy and syncope: at least so Weiss suggests. Vaso-vagal syncope of Weiss and Ferris has a somewhat similar mechanism to that of the cardiac type of carotid sinus syncope. This very occasional form of syncope is due to reflex slowing of the heart caused by gastro-intestinal disorders acting through the vagus nerves. Night starts and bad dreams are more common in the subjects of aortic than of mitral disease. But a story of night starts and bad dreams is not infrequently told by an emotional and imaginative patient such as this one. Palpitation too is not uncommon in the subjects of aortic disease, but here again the sensitivity of the nervous system greatly conditions its occurrence. The asthenia complained of is unassociated with heart failure or with active valvulitis. The latter would be evidenced by the leucocyte count (best of all), the pulse rate especially the sleeping pulse rate over 90, temperature above 99°F., accelerated sedimentation rate, dyspnoea, præcordial pain, nausea and vomiting, by rheumatic polyarthritis, twitching, nodules, muscle and joint pains, hæmoptysis, diarrhoea and petechiæ, progress of valvular lesions, electrocardiographic changes and increasing heart size. We may therefore reasonably conclude that this case is complicated by neurocirculatory asthenia.

The slight pallor of this patient is unattended by appreciable anæmia. Active rheumatism has been excluded. Subacute bacterial endocarditis is negated by the absence of symptoms and signs of infection including finger clubbing, splenic enlargement and superficial petechiæ. Another possibility is 'pale mitral stenosis', *i.e.*, mitral stenosis

associated with aortic regurgitation. Neck pulsation, however, is absent. But the slow heaving cardiac impulse is a striking sign: in view of the absence of neck pulsation it prompts a diagnosis of aortic stenosis. This diagnosis is confirmed by the presence of the corresponding murmur and thrill, diminished aortic second sound, aortic diastolic murmur, moderately enlarged left ventricle, and by the absence of aortic dilatation radiologically. The presence of mitral stenosis further reinforces the diagnosis. The pulse is a compromise between the pulses of all three valvular lesions. A rheumatic ætiology is clearly indicated by the rheumatic history, prominent præcordium, clinically and radiologically evident mitral stenosis, and the electrocardiographic picture. We shall now briefly interpret the latter.

Auricular hypertrophy, the logical consequence of mitral stenosis, is evidenced by the excessive height and width of P. Ventricular preponderance is lacking in this case of rheumatic aortic stenosis and regurgitation with mitral stenosis,



Electrocardiogram of case reported.

types, (1) cardiac or circulatory, and (2) cerebral (Ferris, Capps and Weiss, 1935). In vaso-vagal syncope, loss of consciousness is secondary to the steep fall of blood pressure, and the vagal slowing of the heart is less important, whereas in the cardiac type of carotid sinus syncope unconsciousness is dependent upon slowing of the heart, which may amount to complete block for a few beats, and the usually accompanying fall of blood pressure is secondary to this slowing of the heart. Sweating aids recognition of the former type of syncope: in cardiac syncope sweating is rare.

The cerebral type of carotid sinus syncope is characterized by the occurrence of syncope and convulsion in spite of the fact that there is no cardiac slowing and no fall in the blood pressure, *i.e.*, in spite of a normal blood flow. Syncope of this type is due to altered reaction of the brain cells, dependent upon vaso-motor changes in strictly localized areas or upon a response to afferent nervous impulses originating in the (hypersensitive) carotid sinuses. Apparently

because the effect of right ventricular hypertrophy associated with mitral stenosis is neutralized by the effect of hypertrophy of the left ventricle which has resulted from aortic stenosis and regurgitation. The cessation of rheumatic activity is marked by the return of the Q-T interval to normal. The P-R interval, however, remains prolonged. Such persistent prolongation of the P-R interval in a rheumatic subject indicates a distinct proclivity to the development of auricular fibrillation, the onset of which is precipitated by the simultaneous action of two factors, *i.e.*, vagal activity and the E factor of Nahum and Hoff. The QRS and P-wave changes tend to persist and will increase with further recurrence of rheumatic activity and the hypertrophies resulting from the diseased aortic and mitral valves. Permanent electrocardiographic changes in rheumatic heart disease include notching or slurring of the QRS group in two or more leads, T-wave inversion ( $T_1$   $T_2$ ) and auricular fibrillation. T-wave changes and factors influencing the pattern of the T-wave in aortic stenosis are already described.

#### *Supplementary note*

Since the completion of this paper the patient has been readmitted on account of a rheumatic relapse. His aortic stenosis is clear-cut as before. His mitral stenosis is more in evidence than formerly, in that he now displays a diastolic thrill, snappy mitral first sound and a longer mitral diastolic murmur. His pulses have altered somewhat. His present blood pressure is 130/90 right arm and 120/75 left arm. The jugular chain of cervical lymphatic glands is just palpable bilaterally. Graded pressure over his right carotid sinus again failed to elicit evidence of carotid sinus sensitivity, such as may be induced to the point of syncope in a chronic dysenteric in our wards, a Hindu male, aged 60 years, who has never in his life complained of dizziness, giddiness or syncope. The vaso-vagal attacks described by John Ryle (1939) emphasize the great importance of nervous impulses in the production of syncope and serve to remind us that cerebral anoxia is not the only mechanism causing unconsciousness in man.

#### *A few points in the treatment of calcific aortic stenosis in the stage of failure*

Bedford (1939) has ably outlined the treatment of isolated left ventricular failure. Mackenzie and Lewis believed that depression of auriculo-ventricular conduction was the essential action of digitalis on the heart. In his treatment of failure with congestion, Lewis said: 'The most emphatic action of digitalis and its allies is in the case of auricular fibrillation'. Lewis (1937) dismissed digitalis therapy in failure with regular rhythm, with the remark that: 'Occasionally, however, cases of chronic congestion that present regular heart action, and that have been treated by all the usual methods

without success, respond to full doses of digitalis'. Wenckenbach and Christian, on the other hand, attributed the efficiency of digitalis to its effect on myocardial tone and contractility, and on this basis advised its use in all congestive failures. Gavey and John Parkinson assessed the clinical value of digitalis in heart failure with normal sinus rhythm and compared the same with that in auricular fibrillation. Their main conclusions were given in a former paper (Kelly, 1939). The third effect of digitalis on the heart, namely its depression of the pace-making function of the sino-auricular and also of the auriculo-ventricular node with resulting tendency of the heart rate to be lowered, has long interested John Parkinson. In soldiers with cardiac symptoms and a frequent pulse John Parkinson (1917) found the reduction in rate from digitalis 'was almost negligible' and in his recent study of digitalis in failure with normal rhythm he remarks that 'Reduction in rate was not always accompanied by clinical improvement, though improvement was rather more common in the patients who showed it. Some good clinical results were seen without any reduction in rate'. Hence, in the regular rhythm failure of calcific aortic stenosis, which is generally documented by a remarkably slow heart rate, we must not strive after a further reduction of the heart rate: induction of the muscular effect of digitalis and not of its direct sinus action is the object of therapy.

Partial heart block does not contra-indicate the use of digitalis.

Convallan is recommended by Ralph Major and Leger (1939) in lieu of digitalis, should heart block or bundle branch block attend cardiac failure, as it not infrequently does in calcareous disease of the aortic valves. Convallan is a special extract of *Convallaria majalis* or lily-of-the-valley. Its activity is due to certain digitalis-like glucosides. Its pharmacological action in large doses is essentially the same as that of digitalis and strophanthin. In small doses it produces remarkable diuretic effect without causing heart block or increasing the degree of any existing block. Its cumulative action is negligible and it may be given before or after digitalization with complete safety. The minimum effective dose is 3,000 frog units, and up to 12,000 frog units may be administered daily with safety. We have had no personal experience of convallan yet.

'The partnership of a mercurial diuretic with digitalis should govern the treatment of heart failure'—John Parkinson. The former lessens oedema, even of the heart muscle itself, and the latter directly improves myocardial efficiency. Nearly ten years ago Bedford demonstrated the occasional superiority of salyrgan to digitalis in the treatment of heart failure. Salyrgan acts mainly on the kidneys, either directly or indirectly as part of a general vascular effect: Hermann and others suggest that it acts preponderantly through inhibiting

tubular reabsorption. Hence reasonably efficient renal function is essential for salyrgan diuresis, and impaired renal function contraindicates the use of salyrgan or other mercurial diuretic. Obviously, calcific aortic stenosis subjects with sclerotic kidneys are unlikely to respond to salyrgan. Other preparations similar to salyrgan are neptal and mersalyl. Esidrone (Ciba), the sodium salt of pyridine dicarboxy- $\beta$ -mercuri-w-hydroxy-propyl-amide-theophylline, contains 32.2 per cent mercury in non-ionizable form and 28 per cent of theophylline which is bound chemically to the mercury molecule. Mercupurin is another mercury-theophylline compound. Fishberg (1937) enjoins upon us not to give mercurials to moribund patients: 'I have', he said, 'seen them add the *coupe de grace* by producing anuria'. Mercurials lower the venous pressure and so are inadvisable in the shock stage of coronary thrombosis.

The action of mercurial diuretics should be supplemented from time to time by xanthine derivatives. Theopyllin (theocin) according to Fishberg produces diuresis predominantly through increase in renal blood flow with consequent augmentation in glomerular filtration. Its chief compounds are theophylline ethylenediamine (aminophyllin or euphyllin) and theobromine sodium-salicylate (diuretin). Theobromine calcium-salicylate (theocalcin) may sometimes usefully replace diuretin. Animal experiments have probably over-emphasized the additive or synergistic effect of calcium and digitalis on the heart. Wall (1939) found that no untoward reactions followed the intravenous injection of 5 c.cm. of a 20 per cent calcium gluconate solution in congestive failure cases receiving digitalis. He suggests that the calcium so injected is diluted before it reaches the heart by the increased circulating blood volume and slowed circulation of heart failure subjects. In Wall's opinion the danger lies in a sudden increase in calcium-ion concentration in the heart and not in the synergism of calcium and digitalis. Finally, we might add that we find some advantage in 'ringing the changes' on diuretic drugs.

### Summary

1. The modern ætiological concept of calcific aortic stenosis is that the vast majority of cases are clearly rheumatic in origin.

2. The incidence of rheumatic heart disease in our hospital practice was shown and an attempt was made to ascertain the incidence of aortic stenosis from our clinical and post-mortem records.

3. The distinctive symptomatology of calcific aortic stenosis was described.

4. The diagnostic criteria of aortic stenosis were discussed in moderate detail.

5. Calcification of the aortic valve demonstrable by fluoroscopy is indisputable evidence of calcific aortic stenosis.

6. The electrocardiographic and other findings were briefly outlined.

7. The essential requirements for a diagnosis of aortic stenosis were stated and the differentiation of calcific aortic stenosis from arteriosclerosis or coronary heart disease was mentioned.

8. A reference was made to the prognosis of aortic stenosis.

9. The importance of correlating clinical, electrocardiographic and radiological findings in a heart case was stressed.

10. A case of rheumatic aortic stenosis was presented.

11. The treatment of calcific aortic stenosis in the stage of failure was briefly reviewed.

I am grateful to Lieut.-Colonel J. C. De, I.M.S., Superintendent, Medical College Hospitals, Calcutta, for permission to report the case. I acknowledge gratefully the help I received from Dr. A. K. Ahmed, my senior house physician, and from Dr. G. B. Sinha, my medical registrar, in respect of our hospital statistics.

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## OBSERVATIONS ON THE USE OF NICOTINIC ACID IN THE TREATMENT OF PELLAGRA AND ALLIED CONDITIONS

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In September 1937 Elvehjem *et al.* discovered that a single dose of 30 mg. of Eastman Kodak Company nicotinic acid improved the appetite and stopped the diarrhoea in a dog suffering from black tongue; since this date many people have treated human pellagrins with nicotinic acid. Results from this form of treatment have been so successful that nicotinic acid is now established as a specific cure for pellagra.

A large amount of research has been carried out in the United States where pellagra is very common. Smith *et al.* (1937) reported a cure with 60 mg. of nicotinic acid daily for twelve days. The appetite improved after 24 hours and mental improvement was noted after 48 hours. The skin was improved after 3 days.

Spies *et al.* (1938) reported an immediate increase in appetite and cessation of nausea and diarrhoea. Twenty-four hours after administration of nicotinic acid, the tongue became less

sore and salivation diminished. He recommended a full well-balanced diet in addition to nicotinic acid.

Spies and Aring (1938) drew attention to beriberi symptoms in pellagra cases. They found that many pellagrins in the U. S. A. suffered from alcoholic neuritis.

In India cases of pellagra are frequently met with. Rau and Raman (1936) reported 8 cases in Vizagapatam. They carried out blood analysis and found that the blood showed a fairly constant reduction in the albumin fraction.

In March 1939, Napier drew attention to the importance of this disease in India in a detailed description of it, and Sen Gupta, Napier and others (1939) recorded five cases treated in Calcutta. Bajaj (1939) treated one of six cases in the Punjab with nicotinic acid and found it to be 'very helpful in improving the local condition of the mouth and the skin'.

A Hindu agriculturist was treated successfully in Midnapore in July 1939 with six injections of nicotinic acid, and further interest in this form of treatment was aroused by two more cases in the Presidency General Hospital. At the same time it was observed that several other patients, particularly Anglo-Indians, showed some of the symptoms of pellagra though not clinically suffering from that disease. Many of this latter group showed improvement under nicotinic-acid treatment.

Altogether 20 cases were treated with nicotinic acid and for study purposes these were divided into three groups.

- (1) Cases of true pellagra.
- (2) Cases of nicotinic-acid deficiency.
- (3) Miscellaneous cases.

*Cases of true pellagra*

Only three cases were allotted to this group. The distinction, however, between this group of cases and those classified under nicotinic-acid deficiency was mainly one of degree. Patients with marked skin lesions, gastro-intestinal and nervous symptoms were classified as true pellagra cases. Less definite cases were classed as cases of nicotinic-acid deficiency. All three were men between the ages of 30 and 50 years. One was a Hindu agriculturist and the other two were unemployed Anglo-Indians.

Rice was the main article of diet in each case though the Hindu was in the habit of eating fish fairly frequently, and the Anglo-Indians ate meat when they could afford it.

The duration of symptoms varied from 7 months to 12 years. The most severe was case 1: he complained of indigestion, itchiness, and 'insects flying out of his ears' and 'worms crawling in the skin'. His condition became worse each winter but he had managed to do his work till a year ago when fever and diarrhoea left him very thin, and he had to give up his employment as a boiler-maker. He had previously been treated in hospital for gastritis.

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On admission he was found to be 'slightly mental' and his general appearance suggested it (see photo). He was very thin and covered with a pigmented coarse skin which was most marked on the front of his chest, on the face and on the outer aspects of his arms and legs. He had fever and diarrhoea and his knee jerks were markedly exaggerated. He had a very moist tongue with red edges and a pronounced tremor.

He received six daily intramuscular injections of 2 c.cm. nicotinic acid. His appetite improved, he became more alert and his skin began to peel off. After six days' interval he received 2 c.cm. (50 mg.) intravenously followed by daily intravenous injections of 3 c.cm. (75 mg.) of nicotinic acid. This caused his skin to go pink

*Pellagra.*



Fig. 1. Case 1.—A photograph taken about 10 days after admission. The distribution of the skin lesions can be seen. A certain amount of leucoderma is present on the hands.

in the less affected areas and hastened the peeling process. He complained of a burning sensation all over his body. His bowels moved less frequently, his weight began to increase, and he had no more fever. He now received three tablets (150 mg.) three times a day for a month, when the dose was reduced to two tablets thrice daily. He received a total dose of 16,975 mg. of nicotinic acid.

His condition on discharge was very good. He gained 13 lbs. 4 oz. in weight, his appetite was good and his tongue was no longer sore. His skin was practically normal, but when the coarse skin peeled off it left paler skin underneath. His mental state showed a marked improvement and he felt well enough to regain his employment as a boiler-maker.

The two other cases of pellagra were less severe. The Hindu (case 3) improved greatly after 6 intravenous injections of 50 mg. each. The most striking change was in his demeanour. He was a morose silent man on admission but after treatment he became brighter and more inclined to talk. His skin began to peel off but he left before complete cure was obtained.

The third patient in this group (case 2) suffered principally from diarrhoea and emaciation. His skin was not so coarse and pigmented as that of the other two. He had a very sore tongue and achlorhydria.

He was treated for more than 2 months as a case of chronic bacillary dysentery, but showed no improvement until nicotinic acid was administered. This had an almost immediate effect on

*Pellagra.*



Fig. 2.—The same case after treatment with nicotinic acid. Note the increase in weight and appearance of the face. The coarse scaly skin has fallen off and lighter coloured skin is left behind.

the diarrhoea which stopped after five days. He received a total of 2,800 mg. of nicotinic acid.

*Nicotinic-acid deficiency.*—Twelve cases were considered to be suffering from deficiency of nicotinic acid. Seven of these were children and the other five adults. Four were females and eight males. They all belonged to the poorer classes and lived mainly on rice and dāl. Four of them complained of a sore tongue and one boy of 13 (case 9) had a swollen tongue with ulceration round the edges and on the surrounding mucous membrane of the mouth. He improved rapidly under nicotinic-acid treatment.

Gastro-intestinal symptoms were present in seven cases and consisted mainly of slight diarrhoea. In two cases, however, diarrhoea was severe and at times was accompanied by vomiting.

All except one case showed some change in the condition of the skin. In some there was a dryness and sealiness with a certain amount of itching. In others the skin was thickened, pigmented and coarse, the distribution of the pigmentation being symmetrical and usually on the forehead, outer aspects of the arms and legs, and on the chest and neck. Almost invariably the patients attributed these changes to the cold weather and asserted that in the summer their skins became perfectly normal until the next winter.

Symptoms of nervous involvement were often present. In seven cases the knee jerks were exaggerated, in two cases diminished, and in two cases absent. One patient had previously suffered from 'beri-beri' and one Chinese boy had had beri-beri symptoms. He left hospital before

*Nicotinic-acid deficiency.*



Fig. 3. Case 4.—The photograph shows the slight pigmentation and rough skin which is often present in cases of nicotinic-acid deficiency.

completing his treatment. One African negro (case 13) suffered from peripheral neuritis due to alcoholic excess, and had no knee or ankle jerks. A marked tremor of the tongue was noticed in two cases only. The majority of cases were rather dull and apathetic, especially the children.

Fever was present in nearly all cases at some stage of their illness and nearly all cases had lost weight.

*Laboratory investigations*

The cerebro-spinal fluid was examined in five cases. Apart from a reduction in the number of cells present and in the protein in some cases, there was no constant abnormality.

On examination of the urine, porphyrin was found in four cases. Hypochlorhydria was an almost constant feature.

The blood was examined in some detail. In only two cases did the red cells reach the level of 4,000,000 per c.mm. The hæmoglobin remained in most cases between 50 per cent and 60 per cent with a colour index in the region of 0.8.

The Wassermann and van den Bergh tests were always negative.

The blood calcium was slightly reduced in several cases, but the serum albumin and globulin were unaltered.

*Treatment*

Nicotinic acid was given to all cases in varying dosage according to the severity of the case. A usual dose was 6 intravenous injections of 2 c.cm. (50 mg.) of nicotinic acid (Glaxo), followed by nicotinic-acid tablets (50 mg. each) two or three times daily.

In severe cases 4 c.cm. (100 mg.) was given daily intravenously for six to ten days, followed by three tablets (150 mg.) three times a day for 3 weeks.

As hypochromic anæmia was a feature of every case treatment was supplemented with ferrous sulphate gr. iii thrice daily, or 'polyhæmen' tablets six daily. Small doses of thyroid were given in some cases, and all received a mixed well-balanced diet.

As a result of this treatment practically all cases complained of burning and itching in the skin which quickly passed off. In most cases the appetite improved after one or two injections, and there was a marked improvement in their mental attitude. They became brighter and more lively. This was particularly noticeable with children who responded rapidly. Several children became very flushed and almost pink, but this wore off soon and did not appear to worry them. The pulse and temperature remained normal.

Four or five injections were required before any effect was noticed in diarrhoea cases, and the skin lesions were the last to disappear, though sealing commenced early on in treatment. The average gain in weight was 4 pounds during treatment.

*Miscellaneous cases*

Nicotinic acid was administered to five cases suffering from various conditions other than pellagra. One was a Jewess who ate a good mixed diet, including meat and fruit, as well as rice and dāl.

She suffered from scabies with secondary infection which gave rise to an extremely offensive odour due to the pus which oozed from the numerous sores on her fingers, hands and toes. She had suffered from this condition off and on for one year. She received 12 intravenous injections of nicotinic acid (600 mg.) and 4,700 mg. by mouth. The skin of her fingers peeled off

Case number	Sex	Age, years	Nationality	Diet	Duration, years	Gastro-intestinal symptoms	Skin lesions	Nervous symptoms	Seasonal exacerbation	Blood counts
I	M.	30	A.-I.	Rice, dāl.	12	Sore tongue, salivation, vomiting, diarrhoea.	Face, chest, abdomen, shoulders, arms, thighs, legs, dorsum of feet.	Hallucinations, tremor of tongue, plus knee jerks, ankle clonus, diplopia.	Winter	R. B. C. 2,230,000, W. B. C. 8,000, Hb. 38%.
II	M.	44	A.-I.	Rice, dāl.	7/12	Sore tongue, salivation, diarrhoea.	Legs, knees, arms, forehead.	Dull, apathetic, absent knee jerks.	..	R. B. C. 3,390,000, Hb. 60%.
III	M.	50	H.	Rice, fish.	3	Sore tongue, diarrhoea.	Neck, forehead, arms, legs.	Headache, morose, dull, plus knee jerks.	Winter	..
IV	F.	9	A.-I.	Rice, dāl.	6	Salivation, vomiting, diarrhoea.	Legs, arms, forehead.	Tremor of tongue, plus knee jerks.	Winter	R. B. C. 3,640,000, W. B. C. 10,200, Hb. 60%.
V	F.	5	A.-I.	Rice, dāl.	2	Vomiting, diarrhoea.	Forehead, arms, legs, back.	Listless, plus knee jerks.	Winter	R. B. C. 3,280,000, W. B. C. 4,250, Hb. 55%.
VI	F.	29	A.-I., sister of No. I.	Rice, dāl.	3	Sore tongue, salivation.	Forearms, legs, thighs.	Headache, sleeplessness, plus knee jerks, ankle clonus.	Winter	R. B. C. 3,640,000, W. B. C. 6,750, Hb. 55%.
VII	M.	11	A.-I.	Rice, dāl, meat.	1	Salivation, vomiting.	Forehead, arms, legs, dorsum of feet.	Knee jerks diminished.	..	R. B. C. 3,240,000, W. B. C. 5,600, Hb. 55%.
VIII	M.	55	A.-I.	Rice, dāl, tapioca, sago.	12	Sore tongue, salivation, vomiting, diarrhoea.	Arms, legs, thighs, dorsum of feet.	Apathetic, knee jerks absent, cramps.	Winter	R. B. C. 3,200,000, W. B. C. 9,750, Hb. 60%.
IX	M.	13	A.-I.	Rice, dāl, bread.	3	Sore tongue, salivation, diarrhoea.	Arms, legs, ankles.	Dull, tremor of tongue, plus knee jerks, ankle clonus.	Winter	R. B. C. 3,540,000, W. B. C. 7,250, Hb. 60%.
X	M.	12	Chinese	Rice	1½	..	Dry skin, leg pigmented slightly.	Knee jerks absent.	..	R. B. C. 3,510,000, W. B. C. 4,500, Hb. 65%.
XI	F.	1½	A.-I.	Rice dāl, arrow-root.	½	Diarrhoea	Skin slightly dry.	Listless, apathetic, plus knee jerks.	..	R. B. C. 3,640,000, W. B. C. 12,780, Hb. 60%.
XII	M.	1	A.-I.	..	½	..	Arms, legs, face.	Irritable, restless, plus knee jerks, ankle clonus. Absent, knee jerks.	..	R. B. C. 3,260,000, W. B. C. 10,750, Hb. 55%.
XIII	M.	43	African negro.	Fish, rice, dāl, meat.	5	..	Legs, arms, chest.		Winter	W. B. C. 11,500
XIV	M.	39	A.-I.	Rice, dāl.	5	Sore tongue, salivation, diarrhoea.	Dry skin, arms and legs scaly.	Sleeplessness, plus knee jerks.	..	R. B. C. 3,260,000, W. B. C. 7,250, Hb. 60%.
XV	M.	59	A.-I.	Rice, dāl.	1/12	Diarrhoea	Dry skin	Dull, apathetic, sleeplessness.	..	..

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Cerebro-spinal fluid	Porphyrin	Fasting juice	Blood chemistry, per cent	Increase in weight, lb.	Concomitant disease	Treatment, nicotinic acid	Result
No increase in pressure, no cells, total protein 26 mgm., glucose 58 mgm.	—	Free acid 0.07, total acid 0.13.	C. 10.05 mg., P. 6.10 mg., Alb. 3.85 g., Glob. 3.39 g.	13½	..	275 mg. IV, 600 mg. IM, 16,100 mg. oral, total 16,975 mg.	Cured.
No increase in pressure, no cells, total protein 15 mg. %, glucose 55 mg. %.	+	No acid	C. 9.33 mg.	10	..	1,600 mg. IV, 1,200 mg. oral, total 2,800 mg.	Cured.
..	..	..	..	..	..	300 mg. IV	Improved.
No increase in pressure, few R. B. C.	—	..	C. 8.96 mg., P. 4.76 mg., Alb. 3.9 g., Glob. 3.16 g.	4½	Malaria (M. T.).	525 mg. IV	Cured.
No increase in pressure, no cells, total protein 24 mg. %, glucose 49 mg. %.	..	..	C. 8.85 mg., P. 4.9 mg.	4½	Kala-azar	150 mg. IV	Cured.
No increase in pressure, no cells, total protein 17 mg. %, glucose 55 mg. %.	—	Trace of acid	..	..	..	500 mg. IV	Cured.
No increase in pressure, no cells.	+	Free acid 0.07, total acid 0.12.	C. 8.29 mg., P. 5.0 mg., Alb. 3.84 g., Glob. 3.0 g.	2	Malaria (M. T.).	300 mg. IV	Cured.
..	—	Free acid 0.01, total acid 0.03.	C. 9.26 mg., P. 6.07 mg., Alb. 4.06 g., Glob. 3.0 g.	11	Prostatic hypertrophy.	900 mg. IV	Improved.
No increase in pressure, R. B. C., W. B. C.: total protein 20 mg., glucose 50 mg.	+	Free acid 0.19, total acid 0.25.	Alb. 3.92 g., Glob. 3.16 g.	7½	..	600 mg. IV, 2,300 mg. oral, total 3,900 mg.	Cured.
..	—	Free acid 0.07, total acid 0.09.	C. 8.95 mg., P. 4.0 mg., Alb. 4.09 g., Glob. 3.00 g.	..	Beri-beri	300 mg. IV	Left before treatment completed.
..	—	..	Alb. 3.96 g., Glob. 2.87 g.	1	..	150 mg. IV, 1,650 mg. oral, total 1,800 mg.	Cured.
..	—	..	..	1	..	150 mg. IV, 250 mg. oral, total 400 mg.	Improved.
..	—	No acid	C. 8.35 mg., P. 6.18 mg., Alb. 4.3 g., Glob. 3.16 g.	..	..	350 mg. IV	Cured.
..	+	..	C. 10.26 mg., P. 5.7 mg., Alb. 4.3 g., Glob. 3.15 g.	7	..	300 mg. IV, 6,300 mg. oral, total 6,600 mg.	Improved.
..	..	..	..	2	..	300 mg. IV	Improved.

TABLE

Case number	Sex	Age, years	Nationality	Diet	Duration, years	Gastro-intestinal symptoms	Skin lesions	Nervous symptoms	Seasonal exacerbation	Blood counts
XVI	F.	25	Jewess	Rice, dāl.	1	Vomiting	Hands, feet.	Dull, apathetic, headache, sleeplessness, plus knee jerks, ankle clonus.	Winter	R. B. C. 3,280,000, W. B. C. 10,250, Hb. 55%.
XVII	M.	52	A.-I.	Meat, fruit, rice, eggs.	3/365	Diarrhoea	Dry skin	Dull, apathetic.	..	R. B. C. 4,020,000, W. B. C. 10,750, Hb. 70%.
XVIII	M.	2	H.	Rice, dāl.	1/12	..	Buttock, chest, limbs.	Irritable, reflexes normal.	..	R. B. C. 3,860,000, W. B. C. 8,750, Hb. 65%.
XIX	F.	26	A.-I.	Rice, dāl, fish.	1½	..	Erythema and blisters all over.	Simple hysterical, reflexes normal.	..	R. B. C. 4,020,000, W. B. C. 7,750, Hb. 70%.
XX	F.	3	A.-I.	Rice, dāl.	1½	..	Dry skin	Listless, reflexes normal.	..	R. B. C. 3,280,000, W. B. C. 14,250, Hb. 60%.

H. = Hindu.

A.-I. = Anglo-Indian.

like a glove and left a healthy skin underneath. The same process occurred with her toes but some of the sores on her hands required touching with iodine to keep them from reinfesting the whole skin.

The remaining cases were two children of which one was a Bengalee, one Anglo-Indian male of 52 years, and one female of 26 years. The Bengalee child had an ulcer on his buttock and scabies with secondary infection. It improved temporarily on receiving nicotinic acid but relapsed and was removed by its father as he was going on leave. The other child had a dry skin and was dull and apathetic. Her general condition improved with nicotinic acid, and she became brighter and more interested in her surroundings. The Anglo-Indian male suffered from a septic scrotum and scabies. He had no appetite and was very apathetic. His appetite improved with nicotinic acid and he became more alert. The adult female suffered from rheumatism. She showed no improvement under nicotinic-acid treatment.

#### Summary and conclusions

1. A description is given of 20 cases treated with nicotinic acid. The successful treatment of three cases of pellagra is described.

2. It is suggested that, though pellagra is quite a common disease in Bengal, there are a much larger group of cases, especially amongst Anglo-Indians, showing such symptoms as sore tongue, anorexia, stomatitis, diarrhoea, and

mental dullness, which respond well to treatment with nicotinic acid. These are classified as cases of nicotinic-acid deficiency for the purposes of this study.

3. It is suggested that certain skin conditions such as infected scabies show improvement with nicotinic-acid treatment which increases the blood supply of the affected area.

4. Treatment with nicotinic acid consisted generally in a course of six intravenous injections of 2 c.cm. followed by two tablets thrice daily. This treatment was combined with the administration of ferrous sulphate and a mixed well-balanced diet.

5. Hypochlorhydria and a hypochromic anaemia were invariable accompaniments. In some cases a reduction in the albumin content of the cerebro-spinal fluid was noted.

*Acknowledgments.*—I wish to thank Major J. C. Drummond, I.M.S., Superintendent, Presidency General Hospital, for permission to publish this article, also Mr. S. N. Paul, Dr. G. P. Khan and Dr. P. N. Ghosh for the laboratory work.

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—concl'd.

Cerebro-spinal fluid	Porphy-rin	Fasting juice	Blood chemistry, per cent	Increase in weight, lb.	Concomitant disease	Treatment, nicotinic acid	RESULT
..	Trace	..	C. 10.0 mg., P. 5.7 mg., Alb. 4.09 g., Glob. 3.0 g.	2	Dermatitis	600 mg. IV, 4,700 mg. oral, total 5,300 mg.	Cured.
..	—	Free acid 0.09, total acid 0.13.	Alb. 4.12 g., Glob. 3.0 g.	..	Ulcerated scrotum.	300 mg. IV	Cured.
..	—	..	..	1	Infected scabies.	3,000 mg. oral	Improved.
..	—	Trace of acid	C. 8.9 mg., P. 4.0 mg., Alb. 4.19 g., Glob. 3.0 g.	1	Rheumatism	300 mg. IV, 1,200 mg. oral, total 1,500 mg.	No improvement..
..	—	..	Alb. 3.96 g., Glob. 3.0 g.	..	Otitis media	150 mg. IV, 1,200 mg. oral, total 1,350 mg.	Improved.

C. = Calcium.

P. = Phosphorus.

IV = Intravenous.

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## EXPERIENCE WITH DISEASES OF THE GALL-BLADDER

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For a long time it has been the general belief that diseases of the gall-bladder are of rare occurrence, are of a serious nature, occur only in elderly women, and are always associated with stones. The obsolete adage 'fair, fat, forty and fertile' is still committed to memory and quoted by medical students, and even by some medical men. However, by experience one finds that lesions of the gall-bladder are as common as, or perhaps more common than, lesions of the duodenum and the appendix, but, as the lesions of the two latter organs produce more acute symptoms for which the patient seeks the doctor's advice, they are noticed more by the surgeon and thought of primarily. In a good many cases symptoms due to gall-bladder disease are attributed not only to other abdominal viscera, such as the duodenum, appendix and kidney, but to extra-abdominal organs as well, especially the heart.

*Ætiology and pathology of cholecystitis.*—Pathological conditions of the gall-bladder that have any surgical significance are intramural, and the avenues of infection are mainly through the vascular and lymphatic systems, though rarely an ascending infection through the duodenum and the bile ducts is possible. Streptococci, staphylococci, *B. coli*, and *B. typhosus* have been found in cultures made from the bile in cholecystitis. Experimentally it has been found that when streptococci are injected into the bile, no change results. But when streptococci are injected intramurally into the gall-bladder a typical cholecystitis develops within a couple of months. In a good many cases the primary infection is in the gastro-intestinal canal, especially in the appendix or the gastro-duodenal area, and the gall-bladder is secondarily affected. The organ may also be affected from the liver by direct contact, in those cases where the liver cells are damaged by continued infection carried to it through the portal system.

The nervous system may also be responsible for the damage to the gall-bladder by the disturbance in the function of the vagus nerve. This may be due to the stimulus which reaches the vagus in its peripheral portion, its centre in the medulla, the mid-brain, and also the inter-brain. The irritation to the vagus may be caused by extrinsic poisons such as nicotine, intrinsic poisons such as a chronically inflamed appendix, or the vegetative impulses which are easily affected by psychological influences in people with a neurotic temperament. According

occurred in a patient who came with severe jaundice and severe pain. The operation was done after the jaundice had disappeared. The gall-bladder was found to be very much enlarged and the liver contained multiple abscesses. Death occurred on the third day after the operation. The third death was in a female patient who started to sink after cholecystectomy, and died on the eighth day, most probably a case of 'liver death'. The fourth occurred in a young man who started persistent bilious vomiting on the third day after the operation and died on the eighth day. Unfortunately, gastric lavage was not done in his case, which perhaps might have saved him. The fifth death was in an alcoholic, in whom a slightly enlarged gall-bladder with nine fairly big faceted stones was removed. He developed persistent hiccough and gradually collapsed on the ninth day (*vide* figure 3).



Fig. 1.—Skiagram showing ptosis and elongation of the gall-bladder.

#### Presentation of cases

**Case 1.**—S. N., male, aged 30. Admitted on 31st December, 1935, for severe pain in the epigastrium, of about six days' duration. Tenderness was present in the right hypochondrium and slight icteroid tinge of the conjunctiva. Patient was extremely debilitated. He was seen first by me in June 1925 for a very severe colicky attack. At that time he was very restless shouting and pressing with his hand on the abdomen and the heart area, and saying that pain was shooting towards the heart. From the way on which he was rolling about and bending down I suspected a colic attack, and from the tenderness in the right hypochondrium with the direction of the radiation of the pain, to the back and the chest, I suspected biliary colic and treated him accordingly. He was reported to be

better, although the pain with radiation to the heart area did not completely disappear. So he consulted a physician who told him that the pain was due to a weak heart, and advised him to take eggs and other nourishing food which made the pain worse. Then he got himself admitted into another hospital and was treated as a kidney case; but as nothing was found in the kidney he was discharged.

On admission, his gall-bladder area was found to be very tender and he showed all the symptoms of acute cholecystitis. He was given an expectant line of treatment, and blood was transfused as his general condition was very low. Cholecystectomy was done after about three weeks. The gall-bladder was found to be pale red in colour, slightly elongated, and covered with fibrous adhesions. The convalescence was rather stormy, and he had severe bilious vomiting with hiccough. Gastric lavage gave complete relief, and the icteric tinge of the conjunctivæ completely disappeared. The course was smooth afterwards. He was discharged on the twelfth day as he felt perfectly well. After about three weeks he returned complaining of severe pain in the epigastrium. For this he was given a mixture containing alkalies and tincture of belladonna. This completely relieved him and since then he has been keeping perfect health, is married, and earning his livelihood as a clerk in a local bank (*vide* figure 1).

In this case gall-bladder pain had been diagnosed and treated as cardiac and kidney pain for nearly ten years. Post-cholecystectomy pain was relieved by an alkaline mixture containing belladonna.

**Case 2.**—Female, aged 25. Admitted on 26th April, 1932, for pain in the gall-bladder area radiating to the back in the interscapular region, for about two years. She had been diagnosed as a case of appendicitis. Radiogram did not show any abnormality of the gall-bladder. On opening the abdomen, the gall-bladder was found to be slightly enlarged, reddish in colour, and covered with adhesions. The cystic duct was embedded in a thick layer of fat. On the fundus of the gall-bladder there was a hard nodular growth of the size of a small pea. The gall-bladder was removed and the patient felt free from pain for about three months. Then she used to complain of pain off and on for about a year. After that the pain completely disappeared. She was in perfect health when seen in 1938.

In this case the gall-bladder was full of adhesions and a small nodular growth was present on the fundus. Cholecystography did not show any pathological condition of the gall-bladder. Post-cholecystectomy pain was present for about one year after which it completely disappeared (*vide* figure 2).

**Case 3.**—Male, aged 31. Admitted in December 1936 for acute abdominal pain of ten days' duration. Had similar attack of pain starting suddenly one year ago. After that it recurred four or five times. Tenderness in the gall-bladder region with slight jaundice. On opening the abdomen the gall-bladder was found to be very much contracted, pale grey in colour, and covered with adhesions. The cystic artery was first ligated. The serous coat was firmly adherent to the viscous, and could not be separated. While isolating the cystic duct, a thick blood vessel—most probably a branch of the hepatic artery—was found passing alongside the cystic duct, toward the fundus of the gall-bladder. It was tied and divided along with the cystic duct, and the gall-bladder was detached from the liver bed. The fundus was firmly adherent to the liver and had to be removed piece-meal. At this point the aberrant branch of the hepatic artery was found to be embedded in the wall of the gall-bladder, and passing on to the right lobe of the liver. According to Reginald Jackson, in rare cases the right hepatic artery runs parallel to the cystic duct and then arches

PLATE IV

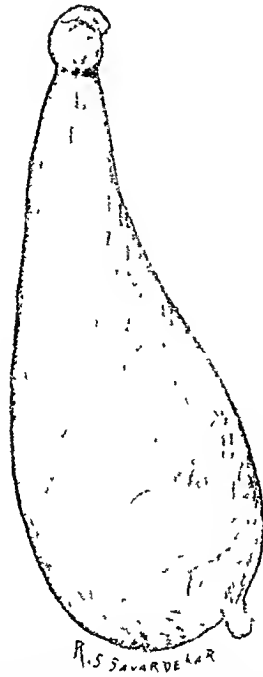


Fig. 2.—Gall-bladder slightly enlarged and having a small papillomatous growth at the fundus.

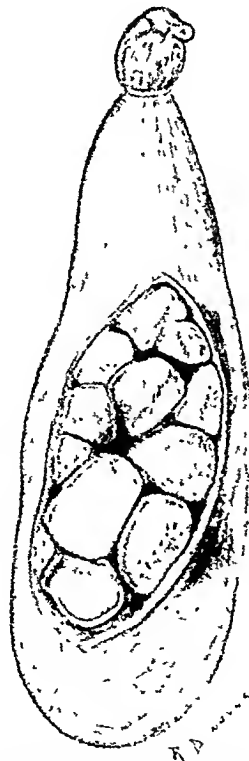


Fig. 3.—Gall-bladder is enlarged and contains numerous faceted calculi.



behind it, at the neck of the gall-bladder. But if the right hepatic artery had been ligated, it would have given rise to some severe complications due to deprivation of the blood supply to the right lobe of the liver. But in this case no post-operative complications occurred, and the convalescence was smooth. The patient was discharged in good condition, and was found to be in sound health some months later.

In this case the aberrant blood vessel passing through the wall of the gall-bladder might have caused the pathological condition of the gall-bladder (*vide* figure 4).

**Case 4.**—Male, aged 24. Admitted in January 1937 for severe pain in the epigastrium and vomiting, which according to the patient contained blood. About eighteen months before he got severe abdominal pain with hæmatemesis, and had the operation of gastro-jejunostomy done on him in another hospital, as a case of duodenal ulcer. He felt perfectly well for about six months. But after that severe abdominal pain and vomiting reappeared. He was a heavy smoker and used to take alcohol frequently. He was suspected to have

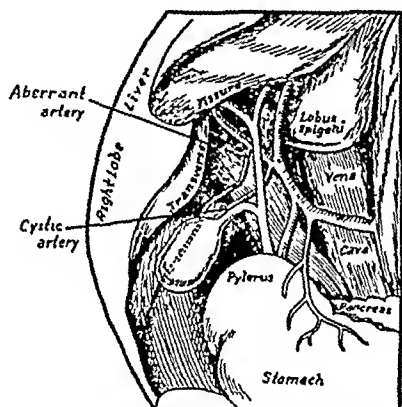


Fig. 4.—Gall-bladder, atrophied, thickened, and changed in colour. The aberrant artery is shown as a branch of the right hepatic artery, going through the wall of the gall-bladder, and entering the right lobe of the liver.

developed a jejunal ulcer. But on clinical and radiological examination, jejunal ulcer was excluded. Cholecystography showed non-filling of the gall-bladder. The gall-bladder area was very tender, especially during the presence of the pain. A very significant thing that was noticed was that Westphal's syndrome was well marked when symptoms of pain and tenderness were present, and noticeably absent during the quiescent period.

On opening the abdomen the gall-bladder was found to be much enlarged, and involved in adhesions. The colour was normal and Lund's sentinel gland could not be detected. The cystic duct was very much narrowed, elongated, and surrounded by thick fibrous adhesions. The gall-bladder was removed. Convalescence was smooth and the patient was discharged free from all symptoms. Since then he has been keeping good health.

In this case the symptoms were most probably due to fibrous contraction of the cystic duct, giving rise to spasm of the gall-bladder. The presence of Westphal's syndrome during the pain and its absence otherwise is rather significant. According to Nathan A. Womack

'Beneath the muscularis in the wall of the gall-bladder, one often encounters single ganglion cells, and at other times relatively large ganglia. These probably

represent vagal pathways. The pain fibres to the biliary tract extend along the hepatic and cystic artery. These fibres extend through the musculature and apparently terminate in the mucosa or possibly between the epithelial cells of the mucosa. These fibres have no specialized endings, but terminate as exposed raw nerve fibres. The pathological changes associated with the nerves of the gall-bladder consist for the most part of fibrosis and inflammation. The lymphocytic reaction is often seen only around the nerve. This may be due to the close proximity of the nerve trunks to the lymph channels. Such an area of inflammation is associated with increased irritability on the part of the nerve. The stimulus probably is that of the increased intracystic or intraductal pressure, either due to abnormal closure of the sphincter of Oddi, or due to spasm of the sphincter or duodenum, or some other portion of the biliary tract. The association of pain, nausea and vomiting, with increase in intraductal pressure, has been noted by Schiager, Ivy, and others.'



Fig. 5.—Skiagram showing the gall-bladder much enlarged and containing multiple calculi.

The above symptoms in the patient might have been due to sudden increase in pressure in the intra-biliary tract as a result of muscle spasm. In those patients with severe gall-bladder disease who are not completely relieved of their symptoms after cholecystectomy, it is possible that there is a certain amount of nerve damage around the common duct which is responsible for the symptoms.

**Case 5.**—Male, aged 48. Admitted on 22nd September, 1937, for jaundice, pain over the left iliac fossa, and loose motions with blood and mucus. He gave a history of dysentery two years previously. Dysenteric stools were absent for one year, but for the last three months he had been passing blood and mucus, with pain all over the abdomen, most marked over the left iliac fossa. Jaundice for one month. Right hypochondrium very tender. van den Bergh test positive indicating



some biliary obstruction. The jaundice disappeared after treatment with biliary stimulants, and van den Bergh test became negative. No ova were found in the stools and sigmoidoscopic examination showed no lesion in the rectum. Blood transfusion was done as the patient's condition was very low, and the gall-bladder removed on 30th November, 1937. The gall-bladder was comparatively free from adhesions and there was not much change in the colour of the viscus, but the blood vessels on its surface were very much dilated and the common bile duct was bigger than normal. The convalescence was smooth and the patient was discharged free from all symptoms and very much improved in health.

In this case the most noticeable symptoms were those of colitis, and history of old dysentery was present. Side by side there were symptoms of gall-bladder lesion as well. It is difficult to say if the gall-bladder lesion was secondary to an attack of dysentery or the irritation of the colon was due to a pathological gall-bladder.

*Case 6.*—Male, aged 30. Admitted on 11th December, 1937, for abdominal pain of about two years' duration. Pain started suddenly, was of an intermittent character, and worse after food. For the last two months pain had become very severe. Slight jaundice was present at the time of admission. Patient gave history of having passed blood with urine. X-ray showed no abnormality of the kidneys or the gall-bladder. van den Bergh test was found to be indirect positive. Gall-bladder area was very tender. On opening the abdomen the gall-bladder was found to be slightly enlarged, pale yellowish in colour, and on palpation stones were found to be present inside the organ. Cholecystectomy was done. Convalescence was smooth, except for an attack of parotitis. The patient was discharged free from all symptoms, and much improved in health.

In this case an unusual symptom, *viz.*, blood in the urine, was present, although the lesion was in the gall-bladder. Cholecystography showed a normally functioning gall-bladder, although it contained multiple stones.

*Case 7.*—Male, aged 40. Admitted in October 1938 for severe abdominal pain with jaundice and slight fever. Morphine was tried for the pain without any benefit. Glyceryl trinitrate tablets were also ineffective. So the homœopathic drug 107-1 mentioned above was given, and it completely relieved the pain, and the jaundice also gradually disappeared. The gall-bladder, which was much atrophied and friable and contained a number of small stones of mixed variety, was removed. The patient was discharged free from all symptoms.

*Case 8.*—Male, aged 42. Admitted in December 1938 for operation of hydrocele. He was very healthy looking, but he complained that he was getting repeated attacks of angina pectoris. He had been diagnosed as a case of pseudo-angina, as the physicians could not find anything wrong with the heart clinically. He got such an attack while convalescing from the hydrocele operation. He complained of very severe pain in the heart area, and was found lying quiet in the bed with his hand on the chest, resenting any interference. There was no change in the pulse, nor was there any dyspnoea. The attack lasted for about seven minutes. No residual symptoms could be detected after the pain disappeared. On examination well-marked tenderness was found in the gall-bladder area and the epigastrium, but nothing abnormal could be detected in the pre-cordial region. Westphal's syndrome was positive. On being questioned about the history of the disease, the patient said that about eight years previously, when the province of Gujrat suffered from severe floods, he had to live for some weeks on the second story of his house in the flooded area of his village. The stay in

the damp atmosphere caused severe gastro-intestinal trouble, from which he suffered for some months. Since then he had been getting these so-called anginal attacks.

Most probably this was a case of chronic cholecystitis giving rise to attacks of pain resembling angina pectoris. Unfortunately the diagnosis could not be confirmed as the patient did not submit to further investigation. The coronary arteries are activated by a pathological gall-bladder. The other theory is that there is a disturbance in the viscerosensory reflex. Irritation of the spinal nerves due to the disease of the gall-bladder is carried to the sensory plexus supplying the aorta and the coronary vessels, producing pain of angina pectoris. Cases have been quoted in which surgical treatment of the gall-bladder has been followed by relief of cardiac pain. A study of morbid anatomy reveals the fact that in subjects with disease of the gall-bladder, the degree of arterial degeneration is higher than in those with normal gall-bladder. So it would appear to be rational to deal thoroughly with cases of cholecystitis or gall-stones as soon as diagnosed.

#### Summary

1. Gall-bladder diseases are very common in India, although stones in the gall-bladder are comparatively rarer than in the West.

2. The majority of patients with cholecystitis gave a history of an attack of typhoid or dysentery and some sort of irregularity in their mode of diet, such as long intervals between meals, absence of fats, etc. Alcohol was responsible for the pathological condition of the gall-bladder in about 10 cases.

3. Gall-bladder pain may be due in many cases to disturbances in the nervous system particularly vagotonia, without any pathological condition of the gall-bladder being present.

4. Meat diet was not found to be an important ætiological factor in cholecystitis, as many of the patients were pure vegetarians.

5. Pathological conditions of the gall-bladder may give rise to symptoms of angina pectoris and may in advanced cases cause degeneration of the heart muscle and of the whole arterial system.

6. After cholecystectomy post-operative pain is very common, and may occur for some months. It usually disappears with belladonna and some alkaline mixture.

7. Jaundice is not a very common complication of gall-bladder disease, nor is pain in the right shoulder. But pain in the angle of the right scapula is often present.

8. The presence of Westphal's syndrome is diagnostic of gall-bladder disease, but its absence does not exclude lesion of the gall-bladder.

9. Cholecystography cannot always be depended upon in diagnosing pathological conditions of the gall-bladder.

(Continued at foot of opposite page)

THE ADULT OF *MICROFILARIA MALAYI*  
BRUG, 1927

By S. SUNDAR RAO, L.M.P.

and

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(From the Diacanthiasis and Filariasis Inquiry under  
the Indian Research Fund Association, School of  
Tropical Medicine, Calcutta)

FILARIAL infection in North Travancore is caused by the adult of *Microfilaria malayi* (Iyengar, 1938). One of us (S. S. R.) carried out field-work recently in this area with the object of isolating adult parasites of this infection, as they have not so far been described. One patient in Shertalai area showed a cyst on the right forearm which was suspected to be of filarial origin. The blood examination of this patient showed *Mf. malayi*. The cyst was aspirated and four adult worms were obtained with lymph. The lymph from the cyst was full of embryos which on examination were found to be *Mf. malayi*. Neither the blood of the patient nor the lymph showed any *Mf. bancrofti*. The adult worms were transferred immediately to normal saline in a petri dish and were subsequently preserved for detailed examination. Of these worms two were males and the other two females. One of the females was broken by the sharp point of the needle during aspiration, the other specimens were complete.

All the worms were alive and were observed to be somewhat sluggish in their movements in the saline solution unlike *Wuchereria bancrofti*, which move actively with a screw-like movement in normal saline, and live for several hours outside the human host. These worms did not show much activity even after warming the saline to body temperature (37°C.) and they died after about half an hour.

In general appearance they are similar to *Wuchereria bancrofti*. The adults of *Mf. malayi* are fine thread-like, white worms, both the sexes living coiled together in the dilated lymphatics. The tapering anterior end shows a rounded head

and neck, and a mouth without lips. There are two rows of tiny papillae running round the head. The posterior end is spirally curved in the male similar to the tail of *W. bancrofti*. In the female the tail tapers to a bluntly rounded tip. The cuticle is smooth and without any transverse striations.

*Female*.—One complete female worm measured 55 mm. in length with a diameter of 0.16 mm. The mouth is terminal and without appendages or lips. The oesophagus is a thick muscular tube with a narrow lumen measuring 1.38 mm., the intestine is a thin simple tube, which in the complete specimen is not clearly visible, being pressed to one side by the fully-packed uterine tubes. The anal opening is 0.94 mm. from the tip of the tail. The vulval opening is 0.92 mm. from the anterior end in one specimen and 1.04 mm. in the other. This opening is a narrow transverse slit measuring 0.036 mm. The beginning of the vagina is narrow (0.045 mm. long). It begins to widen gradually from this point. The general course of uterus and its branches ending in the ovaries is practically the same as that of *W. bancrofti*.

The ovum varies greatly in size, and generally has an ovate outline, measuring 0.027 mm. long and 0.018 mm. broad. The embryos can be seen doubled up inside the shell and higher up they can be seen in a more advanced stage of development where the length of the embryo is considerably longer.

*Male*.—The worm measures 22 to 23 mm. in length with a diameter of 0.088 mm. The oesophagus is 1.12 mm. long, the alimentary canal is straight and ends in the cloaca. The tail is curved, spirally showing three turns.

There appear to be two pairs of large papillae one immediately in front of and the other just behind the cloaca and in close apposition to them there are two pairs of smaller papillae. No other papillae could be observed. The ventral surface of the worm shows fine transverse corrugations similar to those seen in *W. bancrofti*. The cloaca opens 0.1 to 0.14 mm. from the tip of the tail.

The spicules are dissimilar and unequal. The long spicule measures 0.34 to 0.36 mm. in length; it is composed of a stout basal portion and ends in a fine lash-like portion approximately two-thirds of the total length. The tip shows a small membranous spoon-like expansion. The small spicule is 0.11 to 0.12 mm. in length and is almost uniformly broad from base to tip. It should be noted, however, that when seen from the side in an unextruded state the distal third appears much thinner than the proximal two-thirds and it has a sickle-like curve (figure 1). This appearance has already been noted by us in the case of *W. bancrofti* (Maplestone and Sundar Rao, 1939) and is probably caused by a twist in the spicule to accommodate itself to the curve of the tail when in the retracted position. There is a small boat-shaped gubernaculum.

(Continued from previous page)

10. Chronic inflammation of the gall-bladder is followed by fibrosis of the nerve ganglia incorporated in the wall of an inflamed gall-bladder; and irritation of these ganglia and nerve terminals due to distension of the organ gives rise to the typical gall-bladder pain.

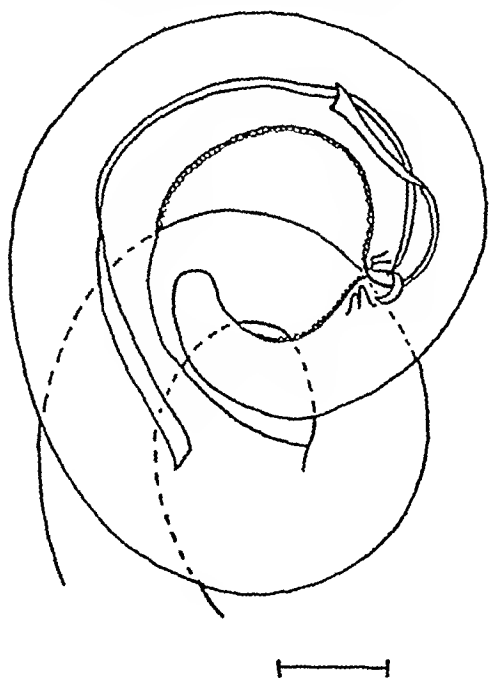
The author's thanks are due to Messrs. R. D. Nayak and R. S. Savardekar, artists, G. S. Medical College, Bombay, for the diagrams published in this article.

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### Discussion

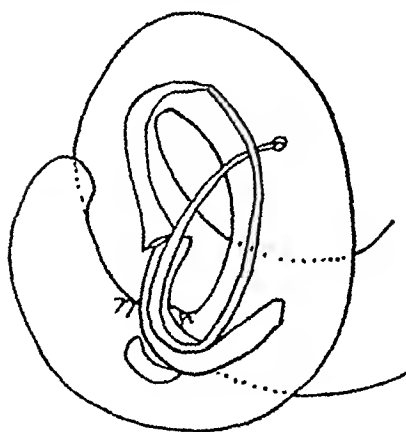
This worm is practically identical with *W. bancrofti* in nearly all its characters. The females are quite indistinguishable.



0.05 mm.

Fig. 1.—*W. malayi* n. sp. Male tail, spicules retracted.

In the case of the males we have had the opportunity over the past few years of examining five or six adult male *W. bancrofti* and are quite satisfied that they possess nine pedunculated caudal papillæ and narrow caudal alæ, but there is a good deal of evidence that these structures show some variation. On account of the discrepancies in the description of the male *W. bancrofti*, which



0.05 mm.

Fig. 2.—*W. malayi* n. sp. Male tail, spicules partly extruded.

Maplestone (1929) discussed, it is probable that the present worm might be considered identical with it, but as we have had the opportunity of comparing the two side by side we are able to distinguish the difference in the tail papillæ. Also, the spicules of the new species are of the same general characteristics, but when seen side by side it is obvious that those of the new species are much more delicate than those of *W. bancrofti* and they also

(Continued at foot of next column)

### A SIMPLE AND INEXPENSIVE FLEA-PROOF CAGE

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Assistant Professor of Bacteriology

(From the Department of Bacteriology and Pathology, School of Tropical Medicine, Calcutta)

A SIMPLE flea-proof cage that can be made in any small workshop and which has been found useful in plague experimental work during the last five years is described. The accompanying diagram illustrates the cage. It is made from an empty kerosene-oil tin. Two glass windows are inserted on opposite sides of the cage, and a platform of wire mesh (4 to the inch) is arranged inside the cage. A removable lid about  $1\frac{1}{2}$  inches deep is prepared. A third of this lid is cut away and fine-meshed (40 to the inch) good quality copper or brass gauze is fixed by soldering, or better still by soldering a strip of tin over the free edges. A shallow (about  $\frac{1}{2}$  inch deep) removable tray is fitted near the bottom of the tin and the box stands on four legs ( $1\frac{1}{2}$  inches long). Two tin tubes are soldered into the lid. One of these tubes is fairly wide (about 1 inch in diameter) to allow the passage down of food and the other narrower for drinking water. There are well-fitting tin caps for these tubes. Below the tubes is a small trough divided into two compartments by a partition, the smaller one being for water and the other for solid food. It is advisable to arrange two small hooks on the wall of the cage into which the trough can be fixed.

The cage can be prepared by any intelligent workman and the whole outfit does not cost more than two rupees. It is advisable to paint the cage with a good quality white paint.

(Continued at foot of opposite page)

(Continued from previous column)

lack the distinct transverse corrugations on the stout portion of the spicules seen in *W. bancrofti*.

These differences are so slight that alone they might be considered insufficient on which to base a new species, but in addition to them there are the differences in the microfilariae which have been recognized for many years and the fact that the insect host appears to be always *Mansonioides annulifera* whereas *W. bancrofti* is known to develop chiefly in *Culex fatigans*. It is accordingly proposed to name the worm *Wuchereria malayi* n. sp. following the name given to the microfilaria by its discoverer.

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## TOPICAL APPLICATION OF SULPHANILAMIDES

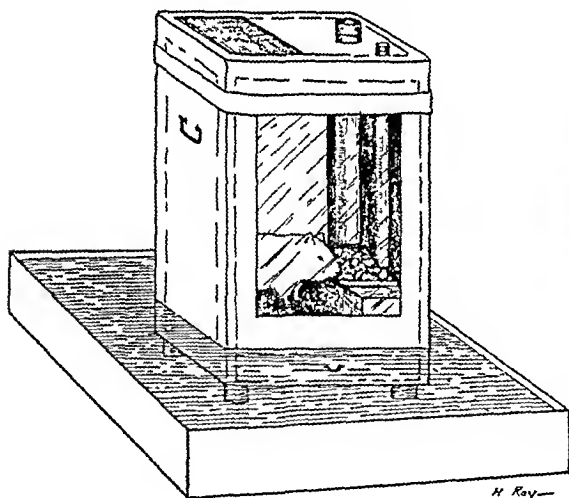
By A. C. DEY, L.M.F.

*Deputy Surgeon, Ashtanga Ayurveda Hospital, Calcutta*

MUCH has been written on the efficacy of sulphanilamide compounds in streptococcal and other bacterial infections when administered by the mouth and parenterally, but I do not think very many publications have appeared in this country on their local use. Jaeger (1936) was the first to write an exhaustive report on the local use of prontosil in a variety of dermatological conditions. The earliest reference to the local use in a case of streptococcal empyema was by Douthwaite (1937) in which 5 c.cm. of prontosil solution was administered through the

*(Continued from previous page)*

For use the cage stands in a shallow trough containing a disinfectant lotion and when the animal has been introduced the space between the flange of the lid and the body of the cage is covered with sticking plaster, which can also be applied over the caps of the tubes soldered into



A simple and inexpensive flea-proof cage.

the lid. The level of water in the trough is well above the removable tray in the bottom of the box. The animal is about  $2\frac{1}{2}$  inches above the water level. Fresh food can be given to the animal through the tubes and any accumulation of excreta can be removed by removing the tray. If desired, a tightly-fitting pledget of wool can be fixed on the top of the food and water tubes. When the animal is dead chloroform is poured in to anaesthetize any fleas that have dropped off from the animal before the cage is opened. After use the whole cage is dipped into a disinfectant lotion or can be boiled in water in a suitable container. A cage can be used several times. The advantages of this cage are that (1) it can be readily made, (2) its cost is minimal, and (3) the animal is visible throughout the experiment.

intrapleural route prior to probable rib resection. This, however, proved to be unnecessary as in three days the pus was thinner and sterile. Subsequently, Brown (1937) reported two similar cases of empyema in which prontosil was inserted into the pleural cavity. These cases were cured without rib resection being necessary. Bosse tried prontosil locally in purulent inflammation of the tonsils and bronchi. He used it in the form of a spray, paint, or gargle, and in tonsillar abscess by injecting prontosil soluble directly into the abscess. Lamers (1938) had good results with local application of prontosil in pyodermic abscesses, furunculosis, erysipelas and herpes zoster. A report of the successful results obtained by inhalation of prontosil soluble in one hundred cases of different kinds of bronchitis is given by Franke (1939). References on the intrathecal and intravenous use of these compounds are also available. As far as the mode of action in local application is concerned, no explanation has yet been put forward by any worker.

Encouraged by these findings, I was tempted to use sulphanilamides for local dressing of wounds in a series of 20 cases. This includes cases of boil, small non-diabetic carbuncle, ulcer, cellulitis, abscess, infected traumatic lesions, and similar minor localized purulent affections. In my trials, urea sulphazide, a sulphanilamide compound marketed by Messrs. Union Drug Co., Ltd., was employed. The preparation was used in the form of a two and a half or five per cent solution and as a five per cent ointment. The usual mode of application was that after the pus was let out by incision the solution was spread over the wound and kept covered with dressings or a gauze soaked with the solution. This process was repeated every day. It has been found that for straight and ordinary cases four to five dressings with a  $2\frac{1}{2}$  per cent solution were sufficient to control the infective process. For the more intractable cases, however, the concentration of the solution was increased to five per cent. As a follow-up treatment, when the purulent discharge had ceased, the ointment was used.

The following are illustrative cases :—

Case 1.—G. C., Hindu male, aged 35 years, developed serotal abscess. Pus was let out by an incision. The first dressing was commenced with a  $2\frac{1}{2}$  per cent solution and changed every day. Altogether eight such dressings were necessary. After that the ointment was applied, at first every alternate day and then every third day. He made an uneventful recovery.

Case 2.—R. L., Hindu male, aged 45 years, developed sub-pectoral abscess on the left side which was incised. The pus pocket was deeply under the muscle. Before insertion of the  $2\frac{1}{2}$  per cent solution, the wound was daily irrigated with normal saline. For four days it failed to show any improvement. From the fifth day onwards a 5 per cent solution was used. The very next day the character and quantity of the discharge seemed improved. Altogether eight more dressings were required. The superficial wound was ultimately dressed with the ointment to effect a cure.

Case 3.—R. G., Hindu male, aged 26 years. He had an axillary abscess. This wound was dressed daily with a  $2\frac{1}{2}$  per cent solution. Altogether ten dressings were

necessary. The ointment was as usual applied to effect a cure.

In none of these cases was any supporting treatment done, except that the margins of the wounds were cleansed with alcohol.

Advantages observed with this dressing are:—

- (1) It is non-irritating.
- (2) Early control of the purulent discharge, and healthy granulation appears quickly.
- (3) It is comparatively non-expensive, particularly with a 2½ per cent solution.

In conclusion, it may be stated that, although it is too early to draw any definite conclusion as to the efficacy of this type of dressing on observation of such a small series of cases, it seems probable that for such minor local infective process local sulphanilamide therapy has some bacteriostatic effect; this renders active assistance to the natural defences of the body to gain the upper hand, and thus helps the regeneration of the damaged and disintegrated tissues.

I desire to express my grateful thanks to Mr. B. Mukerjee, the Deputy Surgeon, Out-patients' Department, Ashtanga Ayurveda Hospital, for his help in conducting trials in some of these cases.

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## A Mirror of Hospital Practice

### PRONTOSIL ALBUM IN GANGRENOUS STOMATITIS

By TEHL RAM

*Sub-Assistant Surgeon, In-charge Civil Dispensary, Banjar, Kangra Dist.*

A MALE child, aged about 10 years, was admitted for frequency of stools with blood and mucus for 20 days, following an attack of measles. The patient was extremely emaciated with subnormal temperature and pulse about 120 per minute. Stools, 20 to 30 in a day, consisted of only blood and mucus. Treatment with emetine, kaolin, bismuth and rectal washes caused the frequency of stools greatly to diminish and blood and mucus was only occasionally seen.

One morning, glossy oedema of the cheeks and feet was observed and on inspecting the mouth cavity, sloughing and foul-smelling black ulcers were found on the outer sides of both upper gums and on the lower gums anteriorly. The sloughing had already involved the whole breadth of gums and the portion affected was quite loose. The case was becoming hopeless. The separated slough being removed, pure nitric acid was applied to the advancing margins and potassium permanganate and hydrogen peroxide solution gargles given. Prontosil album 4 tablets a day were given. Fourteen tablets were given altogether. During this time, oedema of face and feet disappeared, advancement of the ulcers stopped and within about a week the gums became healthy.

The result is remarkable when compared with past experience of such cases which were invariably fatal.

I am indebted to Dr. G. W. Hardy, Civil Surgeon, Kangra, for his permission to publish this note.

### CARDIO-SPASM OF ŒSOPHAGUS

By SUDHIR KUMAR BASU, M.B.

*Assistant Surgeon, E. I. Railway Hospital, Jamalpur*

THE case reported by M. G. Kini in the *Indian Medical Gazette*, January 1939, reminds me of a similar case treated recently at the Jamalpur E. I. Railway Hospital. At first it was wrongly diagnosed as malignant disease of the stomach. The patient belonged to the male sex and was past 40. As, according to Kini, such cases are rare I venture to publish this case, without attempting to explain or discuss it.

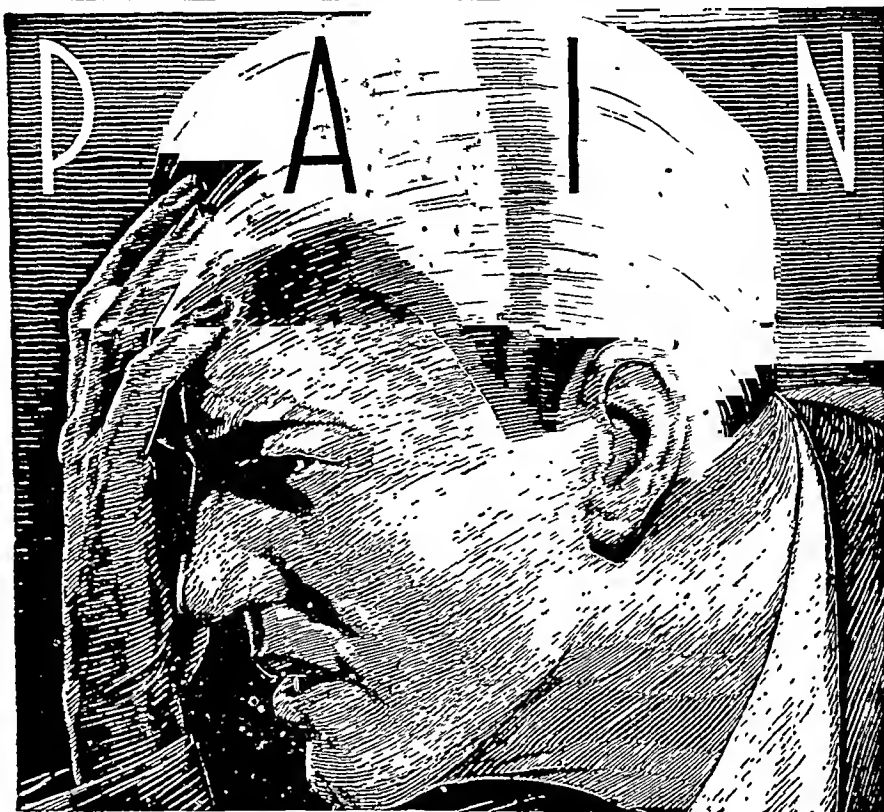
The patient, a Hindu male, aged 42, a workman in the Railway Workshop at Jamalpur, was admitted to the Jamalpur Railway Hospital on 7th December, 1938, for difficulty in swallowing of about two years' duration. There was no history of acidity, indigestion, taking a corrosive or irritant drink, or of having ever suffered from cardiac or respiratory trouble, neither was there any history of syphilis. Considering the history of two years, the patient did not seem to be very emaciated. When asked to drink water, he took some with great difficulty but vomited it in about ten minutes. He could not take dry biscuits and bread but could with great difficulty take a portion of them with sips of water. Palpation did not reveal the presence of any abdominal neoplasm nor could percussion bring forth any abnormal dullness. A stomach tube could not be passed; on taking the tube out its tip was blood-stained. A fluoroscopic examination with contrast meal showed a clear shadow at the upper part of œsophagus without any sign of pressure or obstruction. But as the meal came near the diaphragm the lower part of the œsophagus began to dilate and the shadow changed gradually from tubular to pear-shape till the whole cardiac area was covered. No part of the meal could be seen to pass down into the stomach. The posterior mediastinum was free. There was nothing like the characteristic shadow of a pharyngeal pouch nor any adhesion or constriction at the lower pole of the œsophagus. An injection of atropine sulphate gr. 1/50 was given. In about 15 minutes the meal was seen to pass down to the stomach and the pear-shaped œsophageal shadow disappeared. The behaviour of the shadow at first suggested the existence of a cul-de-sac or some kind of an obstruction at the lower end of the œsophagus, but this suspicion was removed by the effect the injection of atropine had in relieving the condition.

The case was treated for several days with daily injection of atropine sulphate gr. 1/100 before meals followed by a belladonna mixture. Good effect was reported all the time he was in the hospital. He was discharged from the hospital on his own request.

The patient was again screened with a contrast meal on 2nd May, 1939. Though his condition was very much improved he was at times having the same difficulty in swallowing as before.

My thanks are due to Dr. S. C. Chatterjee, the Chief Medical Officer, and Dr. G. E. Paul, the Divisional Medical Officer, E. I. Railway, for allowing me to publish these notes. My thanks are also due to my colleague Dr. S. C. Chowdhury who took a great interest in treating and following up the case.





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# Indian Medical Gazette

MARCH

## HOSPITAL ORGANIZATION IN INDIA I

PROBABLY the most serious check to general medical progress in this country is the inadequacy of hospital organization; the extent of this inadequacy may be judged by the immense area that is served by each hospital, by the smallness of the numbers of beds per head of population, and by the extremely poor quality of the accommodation and attention provided in the hospitals. Some relevant figures are given in an interesting review of the position in India by Colonel Chopra, which will be found elsewhere in this issue, and also in Major-General Bradfield's *Indian Medical Review* published at the end of 1938.

The area served by each dispensary varies considerably, even if we leave out of consideration two exceptional administrative areas—Delhi province with its compact population of over 1,000 per square mile, and a hospital or dispensary for every 24 square miles, and at the other end of the scale the sparsely populated Baluchistan where each hospital or dispensary has to provide for an area more than fifty times as great, 1,327 square miles. In the Central Provinces each hospital or dispensary has to serve an area of 291 square miles against 54 in Bengal. But whilst Bengal heads the list for the number of hospitals and dispensaries, it is obvious that bedless dispensaries predominate, for the average number of beds in these institutions is only 7 against 28 in Bombay, 16 in the Punjab, and 14 in Madras. In Bengal each hospital bed has to serve a population of 5,000 persons and the figure for the whole of India is calculated at 0.3 beds per thousand.

On the matter of the quality of the treatment given to the occupants of these beds, it is difficult to find terms in which this can be measured, as there are so many factors concerned; excluding consideration of the medical personnel, we still have the accommodation, the surgical and other equipment, the nursing, and the diet and general medical comforts. Perhaps the easiest factor to put into figures is the nursing. For the whole of India the number of beds per nurse is 14, or seven nurses per 100 patients; this, after allowance is made for night and day nursing, the administrative and theatre staff, and the leave roster, is a ridiculously small figure. In the teaching institutions in the large cities, the number of nurses per 100 beds is of course much larger, 20 or even 30, which is still far below the British and American standards, but this larger number in the teaching institutions only means that in other hospitals the number of nurses is correspondingly low; in

Bengal as a whole there are 12 beds per nurse, excluding midwives and male nurses, which had they been included would bring the figure down to 9 or 10. In Madras there are 10, and in Bombay just over 9 beds per nurse. It is the frequent complaint of the rural civil surgeon that he dare undertake nothing but emergency or very simple surgical operations because of the total inadequacy of the nursing arrangements.

The hospital is an ancient institution. In early Greek history there are frequent references to hospitals, both as teaching centres and for the care of the sick, and similarly in India there are early historical accounts of the founding of hospitals, for poor and sick. In Europe, even through the Dark Ages, hospitals, which were mainly refuges for the sick and needy, survived and there is a hospital in London still occupying the site which was given to it by Royal Charter in the year 1137. But in India hospitals disappeared for many centuries until they were reintroduced by the British.

At the beginning of the last century, hospitals were not popular and one has only to read the accounts by contemporary writers of the hospitals that existed in those days to understand why. In the pre-Listerian days the total mortality of patients entering hospital was appalling; even if the diseases from which they suffered were easily curable, they usually managed to acquire some other affection, and a woman entering a maternity hospital invariably suffered from sepsis. But with a better understanding of what constituted infectiousness and the introduction of antiseptic and aseptic practices, hospitals ceased to be the death-traps that they undoubtedly were, and, after the natural prejudice against them had gradually disappeared, they became popular and to-day in most advanced countries the demand for hospital treatment far exceeds the accommodation available. The appreciation of the advantages of hospitalization is at its highest in the United States of America (the word itself surely originated on that side of the Atlantic), and in that country few women will choose to be confined in their own homes. The hospital habit is developed far more highly in some European continental countries than it is in Great Britain, where incidentally the war has focused a great deal of attention on the present hospital system with its advantages and disadvantages. But in Great Britain there are about five beds per thousand of the population and even then many patients in need of hospital treatment are turned away. The great advantages of hospital treatment are rapidly being learnt by the people of India. In the larger cities, there is always a waiting list for admission for any but emergency cases, and it has been said facetiously that it requires more influence to get a bed for a hydrocele operation in a certain large Calcutta hospital than to get a seat in the Legislative Assembly; whenever a hospital is not full one

may be sure that there is something wrong inside the hospital walls.

New ideas in medical treatment rapidly seep through to the illiterate ryot who forms the bulk of India's population. A good example is the parenteral injection; 25 years ago the sight of a syringe frightened a patient into absconding from hospital, to-day the same patient thinks he is being unfairly treated if he is only given medicines by the mouth. The hospital idea is firmly implanted in the Indian mind and it will continue to grow. The problem is to meet the increasing demand for hospital accommodation. The tendency is to attribute the lack of hospital accommodation to India's poverty, or alternatively to the failure of the government to do something about it, but the trouble is deeper and goes back further than this.

We will not attempt here to trace the growth of the hospital system in other countries, except to note that in practically all European countries, the first hospitals were founded by religious bodies and were charitable institutions. They were often given the blessings of the government of the day but no more and sometimes less, in that their funds were frequently confiscated. It is from such beginnings that the 'voluntary' hospital system, which until recently was the mainstay of British medicine, evolved. No counterparts, either of these early religious institutions, or of the present voluntary hospitals, exist in India. The first hospitals in this country (within the last millennium) were founded by the British Government or by Christian missionary bodies, and it is only within very recent times that other religious bodies have followed this example.

The government hospitals, in particular, were modelled on the British system, modified to suit Indian conditions, so that they have never had the advantage of natural growth through which process British hospitals have passed. The case of the missionary hospitals is somewhat different; most of these have developed from small beginnings, and though poorer and not so well equipped they are often quite as well suited to the requirements of the people as are the more pretentious government hospitals. Another big group is formed by the municipal and district board hospitals. Nearly all the hospitals in India can be placed in these three groups, and in the country as a whole they each provide about one-third of the beds.

The proportion of hospital beds already provided by the central and provincial governments is far in excess of those provided by the governments in most other countries, and they cannot be expected to provide more, except for special purposes as for example in connection with medical education. It is not really desirable that they should, even if they could afford the money, which in these days they obviously can not. Nor will the problem be solved by Indian philanthropists building large hospitals, on

which their names may be inscribed but which, through lack of endowment and of any local support, remain half empty and even then have to be maintained by government.

In other countries the hospital system has been built up by the people themselves; in this country the beginnings have been made by the government and foreign missionary bodies, the interest has been created, and it is for local enterprise with the aid of local philanthropists to carry on the work. There are many missionary hospitals in India which though started and still helped by funds collected in other countries are now almost self-supporting; by charging fees to those who can afford to pay, they have been enabled to provide free treatment for the really poor and it is on this principle that hospitals of the future will have to be built up. Colonel Chopra, in the paper to which we have already referred, has suggested that the almoner system should be introduced into government hospitals. Something of the kind will have to be done, but it will be difficult to put into effect, for the government is always looked upon as fair game and many, who will conspire to defraud the government by concealing the truth, will hesitate to cheat the local community, and, further, their fellow citizens will see that they do not do so.

Finally, the idea of personal service must be further developed in India. The shortage of nurses is a serious handicap to progress in hospital provision. For many years only Europeans and Anglo-Indians came forward for training as nurses and even now the profession of nursing does not appeal to the educated Indian, but if there is to be any marked improvement in hospital provision a very large body of nurses will be required; these cannot be provided by one community, and the leaders of all communities must endeavour to change the present attitude and encourage their educated young women to take up nursing. That the facilities for training nurses are not ideal is perfectly true, but recently, though efforts have been made to improve these and induce more better-class Indians to take up this profession, the response has been disappointing. Perhaps the most serious obstacle to progress is the poor provision that is made for nurses, both in the matter of pay and of accommodation; it is not a good sign that recently the funds raised for building a new hospital in Calcutta were expended on the provision of an up-to-date hospital building without any balance being left for the nurses' quarters, more particularly in view of the fact that this was a women's hospital and that women were mainly concerned in the organization and management of the fund.

The problem of hospital accommodation in India is not simply an economic one; it will not be solved until the civic conscience is more fully developed, and the people begin to realize that an impressive façade does not compensate for poor medical treatment behind it, that a good

nursing staff is more important than an x-ray apparatus, and above all that the provision of

hospital treatment for the sick is their own local responsibility.

## Special Articles

### HÆMATOLOGICAL TECHNIQUE

#### PART II

By L. EVERARD NAPIER, M.R.C.P. (Lond.)  
and

C. R. DAS GUPTA, M.B. (Cal.), D.T.M.

From the School of Tropical Medicine, Calcutta

#### (3) Enumeration of erythrocytes in the peripheral blood

ERYTHROCYTES and leucocytes are expressed as the number of cells per cubic millimetre (c.mm.) of blood.

*Principle.*—In enumerating the red or white cells, oxalated venous blood from the flask (or capillary blood from the finger or ear lobe) is taken into a red or white cell pipette up to a certain mark, and the pipette is filled with the diluting fluid; it is then shaken, and a drop of the mixture is put into a special counting chamber, where the cells within some specified ruled area are counted, and finally the total number of cells per c.mm. is calculated.

The necessary dexterity to carry out the various manipulations in the different stages of making a blood count can only be acquired by practice. Further, close attention must be paid to every detail of the technique, if accurate results are to be obtained.

#### Apparatus required

- (a) Microscope.
- (b) Hemocytometer with counting chamber, preferably with Neubauer ruling.
- (c) Red and white cell pipettes.
- (d) Coverslip.
- (e) Diluting fluids.
- (f) Watch-glass.

The ideal would be to use certified counting chambers and pipettes, but, where this is not possible on account of their high cost, only those which are manufactured by reliable firms (*viz.*, Carl Zeiss, Bausch and Lomb, etc.) should be used and these should at least be checked against certified instruments.

*Counting chambers.*—There are various types of counting chamber in use. The new types of chamber have two main advantages over the old Thoma chamber:—

(1) The coverslip can be placed in position upon its base before the blood is introduced and this may be done slowly and with the care that is essential to ensure the appearance and persistence of Newton's colour bands at the surfaces in contact.

(2) The uneven distribution of the corpuscles on the counting surface, which is liable to arise in the original chamber devised by Thoma and

is due to the rapidity with which the corpuscles, especially the red ones, tend to settle in the diluent, is obviated; the new chambers are so devised that the diluted blood rapidly enters the counting space by capillary attraction.

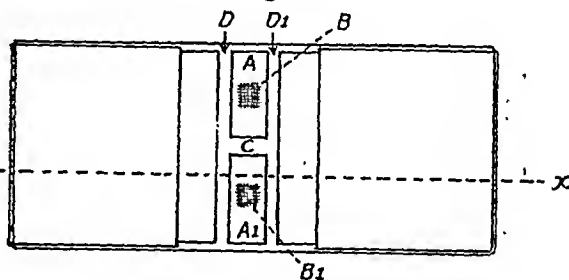
In the new types of chamber, *e.g.*, Neubauer, Bürker, etc., the counting space is oblong and divided into two compartments by a transverse groove, both of which contain a ruled area for counting the red as well as the white corpuscles. These two counting areas afford a means of making duplicate counts with a single application of the coverslip.

In our laboratory we have used chambers with Thoma, Bürker and Neubauer rulings, but for over two years we have been using only chambers with the Neubauer ruling which is simpler to use than the Bürker. With a single application of the coverslip, a larger area for the leucocyte count, four square millimetres on each side of the chamber, as opposed to one square millimetre in the Thoma type, is obtained.

#### Counting chamber with improved Neubauer ruling

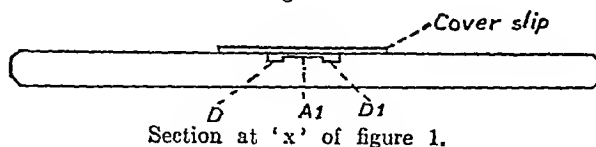
The different parts of the counting chamber are shown in figures 1 and 1a.

Fig. 1.



Improved counting chamber.

Fig. 1a.



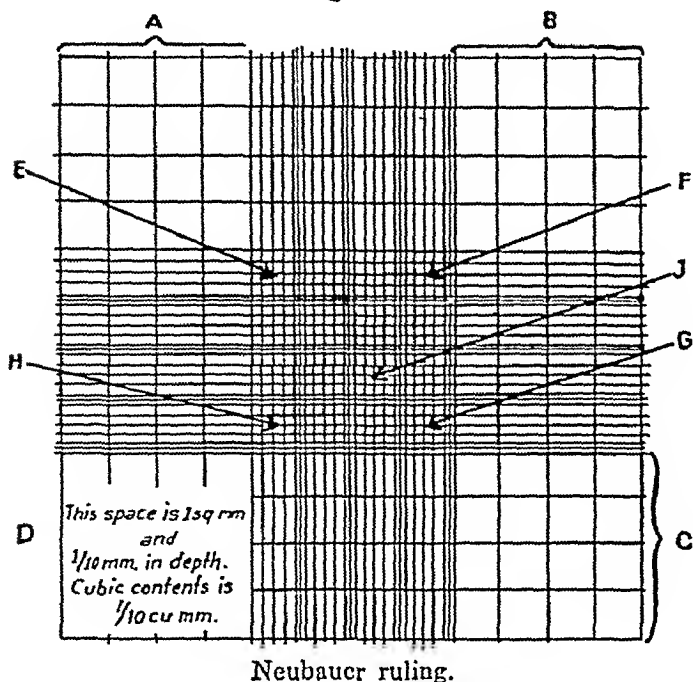
Section at 'x' of figure 1.

The middle platform A-A<sup>1</sup> is exactly 0.1 mm. lower than the two side platforms. When the coverslip is placed upon the platform, there is a space exactly 0.1 millimetre deep between it and the ruled area on the platform. Upon the ruled area, there are nine large squares, one square millimetre each, separated by double lines.

The four large corner squares A, B, C and D, are the areas in which the leucocyte count is

made (figure 2). Each of these four square millimetres is subdivided into sixteen squares to facilitate counting.

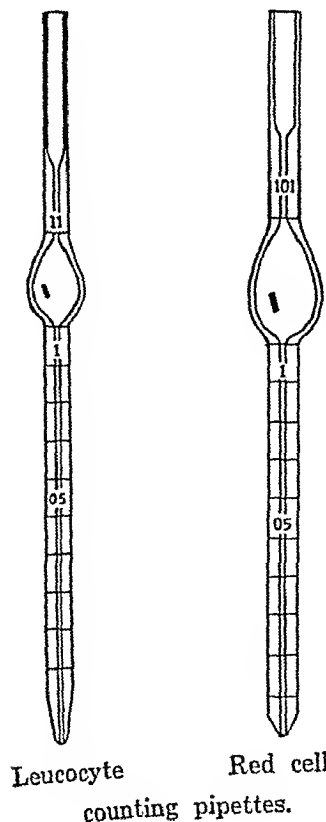
Fig. 2.



The square millimetre in the centre of the ruled area is used for the red cell count. It is subdivided into 400 smaller squares each of which is therefore  $\frac{1}{400}$  of a square millimetre.

To facilitate counting, these 400 small squares are cut up into 16 groups of 16 small squares each, by extra lines which are drawn through every fifth square. Red cells in the five small groups of squares, one from each corner, E, F, G and H and one from the centre, J, that is to say, the contents of 80 small squares in all, are counted.

Fig. 3.



*The coverslip.*—Only the coverslip which is specially designed for blood-counting chambers must be used. If any other coverslip is used there may not be uniform depth in the counting chamber and the count will be inaccurate.

#### *The blood-counting pipettes (Thoma type)*

The capillary portion of both the red and white cell pipettes (figure 3) is divided into ten equal parts from the tip to the bottom of the

bulb, the fifth and the tenth marks being denoted by figures 0.5 and 1, respectively. There is another mark just above the bulb where the figure 101 is given on the red cell pipette and the figure 11 on the white cell pipette.

To facilitate mixing, there is a bead in the bulb, which is sometimes coloured red in the red cell pipette to distinguish it from the white cell pipette.

*Diluting fluids.*—For the red cell count we have found the following solution the most satisfactory :—

Sodium sulphate ..	.. 12.5 grammes
Glacial acetic acid ..	.. 33.3 c.cm.
Distilled water ..	.. 200 "

There is neither clumping nor hæmolysis with this fluid. Other solutions recommended are Hayem's fluid,

(Mercuric chloride ..	.. 0.5 gramme
Sodium chloride ..	.. 1.0 "
Sodium sulphate ..	.. 5.0 grammes
Distilled water ..	.. 200 c.cm.)

and simple physiological salt solution. We have not found either of these satisfactory, as clumping may occur with the former and hæmolysis with the latter solution.

For the white cell count we have found the following solution the best :—

Glacial acetic acid ..	.. 2 c.cm.
Mercuric chloride ..	.. 0.1 gramme
Aniline gentian violet ..	.. one drop
Water ..	.. to 100 c.cm.

The mercuric chloride will prevent growth of moulds when the solution is kept for a long time, and the gentian violet will give a slight tinge to the leucocytes and also make it easy to distinguish this solution from the red-cell-diluting fluid.

When the diluting fluids are used, a small quantity should be put into a watch-glass or other suitable receptacle into which the pipettes charged with blood should be plunged. In no case should the pipettes be put into the original phials containing the diluting fluids, as there is every possibility that in course of time cells will find their way into this fluid and accumulate at the bottom of the phial; these may be taken up subsequently with the diluting fluid and vitiate the count.

#### *Enumeration of erythrocytes*

(i) *Filling the pipette.*—Before using a pipette see that it is absolutely dry and clean and that the point is intact (the tips are easily damaged). With a dry red cell pipette suck blood up to the mark 0.5 (or 1 in the case of anæmic patients) by holding the pipette almost horizontally and at right angles to the line of vision, so that the exact height of the column of blood can be seen easily. The blood should not go much beyond the mark, but, if it does go a little beyond, it is brought back to the mark by applying the tip of the pipette to the tip of the finger a few times; cotton-wool or



blotting paper should never be used as they will draw out the serum only and the cells in the pipette will become more concentrated. The blood adhering to the outside of the pipette is wiped off, and the pipette is plunged into the red-cell-diluting fluid in a watch-glass. The diluting fluid is drawn up exactly to the mark 101, the pipette being held nearly vertical and gently rotated between the thumb and the forefinger. The rubber tube is taken off and a tightly fitting flat rubber band is put on, closing both the ends to prevent any leakage. It is now laid flat on the table, or in the box.

When the pipette is filled, it will be seen that the entire capillary end of the pipette from the tip to mark 1 is occupied by diluting fluid. Hence, the true dilution of the cells is not 0.5 (or 1) in 101, but 0.5 (or 1) in 100, i.e., 1 in 200 (or 1 in 100). Thus, by taking blood up to the different marks from 0.1 to 1 in the pipette, dilutions ranging from 1 in 1,000 to 1 in 100 can be made.

If there be any air bubbles at any stage in filling up the tube with the blood or the diluting fluid, the whole preparation should be rejected and another pipette filled up, for it is never possible to get all the air out without loss of some fluid.

(ii) *Shaking the pipette.*—On every occasion, prior to the charging of the counting chamber with the diluted blood, the pipette should be shaken, preferably in a shaking machine or by rotating the tube, held horizontally, between the palms of the hands, first with the right hand on top and then the left, for about two minutes. The pipette should never be shaken in a horizontal direction, i.e., in the direction of its long axis, as this tends to throw the cells into the capillary tube.

(iii) *Charging the counting chamber.*—The counting chamber and the coverslip must be perfectly clean and free from dust or threads of cotton. Put the coverslip on the counting chamber so that it covers the ruled areas B and B<sup>1</sup> (figure 1), and with the finger nail tap the coverslip to ensure good contact. Discard the first few drops of the diluted blood by blowing into the pipette. Next, holding the pipette in an inclined position of about 45 degrees, apply a small drop of diluted blood to that part of the platform A-A<sup>1</sup> of the counting chamber which just projects from the coverslip; the drop will instantly pass under the coverslip by capillary attraction. The drop of blood should not be too large, or it will overflow the chamber and pass into the overflow trenches D-D<sup>1</sup>, and may even pass to the transverse trench C. Neither should the drop be too small as in that case it will not completely fill the counting surface. With a little practice a drop of the requisite volume can be put under the coverslip; any little excess on the platform should be removed by sucking with the pipette and never with blotting paper.

Small air bubbles are liable to be introduced into the counting chamber together with the diluted blood—

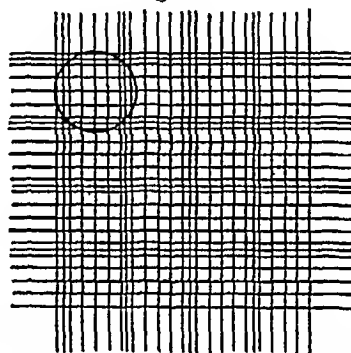
- (i) if the counting surface and the coverslip are not previously cleaned with the requisite care, or
- (ii) if the point of the pipette is chipped.

If there be any overflow into the trenches, or if there are any air bubbles remaining, the chamber must be cleaned and charged again.

#### *Focusing the ruled area*

Great care is necessary in locating the ruled area without injuring the objective or disturbing the distribution of cells. This is most conveniently done by locating the ruled area first with the low power (two-thirds objective and 10 × eyepiece)—lowering the condenser or reducing the light by means of the iris diaphragm will show up the rulings distinctly (figure 4); the higher power (one-sixth objective) may then be substituted by simply rotating the nose piece of the microscope.

Fig. 4.



*Thoma ruling as seen with  $\frac{2}{3}$ rd lens. The black circle shows the field seen with the  $\frac{1}{6}$ th lens.*

#### *Counting the cells*

Place the counting chamber on a horizontal surface for about 2 to 3 minutes to allow the cells to settle properly.

Focus the ruled area with the low power and also find out if the cells are evenly distributed—if not, another preparation should be made.

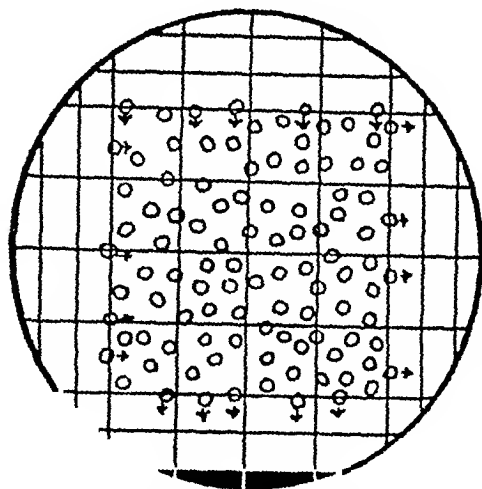
The cells in the squares can now be counted with the high power, one-sixth objective. The area from which the cells are to be counted will vary with the different types of ruling, but the same rule for cells on boundary lines should hold good in all cases.

*Rules for cells on boundary lines.*—All the corpuscles touching the upper line and the left-hand line of a square are considered to be inside the square, while those touching the lower line and the right-hand line of a square are considered to be outside the square (figure 5).

The cells contained on the five groups of small squares E, F, G, H and J in the middle of the ruled area of the Neubauer ruling are counted.

In all cases the cells on both sides of the chamber should be counted and the mean of the two taken. Should there be a difference of more

Fig. 5.



*One field with  $\frac{1}{2}$ th lens showing which cells should be counted and which neglected.*

than 5 per cent in the two counts, the chamber should be recharged and the count done again.

#### Calculations for erythrocyte count

Each small square =  $\frac{1}{100}$  square millimetre.

Therefore, the cubic dimension of each

$$= \frac{1}{100} \times 0.1 \text{ (space between the coverslip and the ruled area)}$$

$$= \frac{1}{1000} \text{ cubic millimetre.}$$

And each group of 16

$$\text{small squares} = \frac{16}{1000} = \frac{1}{62.5} \text{ cubic millimetre.}$$

Therefore, cells from

5 groups of 16

$$\text{squares each} = \frac{5}{62.5} = \frac{1}{12.5} \text{ cubic millimetre of diluted blood.}$$

Thus, the total number of cells counted from 5 groups of small squares multiplied by 50 will give the number of cells in 1 c.mm. of diluted blood.

This, when multiplied by the diluting factor 200 (or 100) will give the number of cells in one cubic millimetre of blood.

*Example.*—Blood is taken up to 0.5 mark.

Total number of cell counted in five groups of 16 small squares = 450.

Therefore  $450 \times 50 = 22,500$  cells per c.mm. of diluted blood;

and  $22,500 \times 200 = 4,500,000$  cells per c.mm. of undiluted blood.

When, as in the above case, blood is taken to the 0.5 mark and the dilution is 1 in 200, the calculation can be simplified by adding four 0's to the total number of cells counted in the five small squares; e.g., in this instance  $450 \times 10,000 = 4,500,000$ .

#### For high counts, as in polycythæmia

One in 200 dilution is not enough as the cells are numerous and would be too crowded to allow

an accurate count to be made, so the blood is drawn up to the 0.2 mark and the diluting fluid as before up to the 101 mark; this produces a dilution of 1 in 500, and the total number of cells in the five squares must be multiplied by 25,000 instead of 10,000 as in the example above.

Conversely, in an anæmic blood it is advisable to take blood up to the 1.0 mark; the dilution will be 1 in 100 and the total number of cells will be multiplied by 5,000.

A table, which will facilitate calculation when blood is taken up to the different marks of the red cell pipette and cells from the five groups of small squares of the Neubauer rulings are counted, is given below:—

TABLE

Blood taken	Dilution	Multiplication factor to arrive at number of cells per c.mm.
0.1 mark	1 : 1,000	$\times 50,000$
0.2 "	1 : 500	$\times 25,000$
0.4 "	1 : 250	$\times 12,500$
0.5 "	1 : 200	$\times 10,000$
1.0 "	1 : 100	$\times 5,000$

*The Thoma ruling.*—The only way this ruling differs from that of the Neubauer is that with the Thoma ruling there are no separate squares for the white cell count, and that there is only one set of rulings instead of two, so that the count cannot be done in duplicate, unless the slide is washed, another drop of diluted blood added, and the coverslip reapplied.

Alternatively, but this does not constitute such a rigid check, a second set of 5 groups of squares can be counted on the same slide, without washing it and reapplying the coverslip.

As the area of the small square is the same as in the Neubauer hæmocytometer, i.e.,  $\frac{1}{4,000}$  square millimetre, the calculations are exactly the same as described above.

#### (4) Enumeration of leucocytes

For enumeration of the leucocytes, follow the technique given under enumeration of erythrocytes, taking all the same precautions in the different steps.

With a dry white cell pipette suck blood up to the mark 0.5 (or 1 in cases of leucopænia), wipe off the blood adhering to the outside of the pipette, plunge it into the white cell diluting fluid and draw the mixture up to the mark 11, take off the tube and put a tightly-fitting flat rubber band round to close both the ends, and keep it flat on the table.

Here, too, the capillary end up to the 1 mark of the pipette is occupied entirely by the diluting fluid. Hence the true dilution of the cells is 0.5 (or 1) in 10, i.e., 1 in 20 (or 1 in 10):

By taking blood up to the different marks from 0.1 to 1 in the pipette, dilutions ranging from 1 in 100 to 1 in 10 can be made.

*Counting the cells and calculation to find out the cells per c.mm.*

*With Neubauer ruling.*—Count the cells in the four corner areas A, B, C and D.

Divide by 4 to get the average number of cells in each area.

We know the area is 1 square millimetre and it is 0.1 millimetre deep.

Therefore the cubic capacity of each area is 0.1 cubic millimetre ( $1 \times 0.1$ ).

Thus, the cells counted are from 0.1 cubic millimetre of diluted blood.

This, when multiplied by 10, gives the number of cells per cubic millimetre of diluted blood. Again, this figure multiplied by the diluting factor 20 (or 10) gives the number of cells per cubic millimetre of whole blood.

*Example.*—Blood was taken up to 0.5 mark.

Number of cells counted from the 4 squares was 120.

Therefore, the average number of cells in 1 square, i.e., in 0.1 cubic millimetre of diluted blood is 30.

Therefore  $300 (30 \times 10)$  is the number of cells in 1 c.mm. of diluted blood; and  $6,000 (300 \times 20)$  is the number of cells per c.mm. of blood.

The number of cells can be calculated rapidly by multiplying the total number of cells from the four squares by  $50 \left( \text{i.e., } \frac{20 \times 10}{4} \right)$  when the dilution is 1 in 20, or by  $25 \left( \text{i.e., } \frac{10 \times 10}{4} \right)$  when the dilution is 1 in 10.

Thus in the above example,

$120 =$  number of cells from the 4 squares

Therefore  $120 \times 50 = 6,000$  is the number of cells per c.mm. of blood.

In cases of leukaemia greater dilution of the blood is necessary for a correct count of the cells, as otherwise the cells are so crowded that an accurate count is practically impossible. In such a case, blood is taken up to the 0.1 or 0.2 mark of a white cell pipette (or up to the 0.5 or 1.0 mark of a red cell pipette) and is filled up with white-cell-diluting fluid. The cells are counted from the 4 big squares as in the ordinary leucocyte count and the number of cells per cubic millimetre is calculated.

A table for facilitating calculation when blood is taken up to the different marks of the pipette, and the cells in four areas of 1 square millimetre each are counted, is given below :—

Blood taken	Dilution	Multiplication factor to arrive at number of cells per c.mm.
0.5 in red cell pipette	1 : 200	$\times 500$
1.0 " " " "	1 : 100	$\times 250$
0.1 " white " "	1 : 100	$\times 250$
0.2 " " " "	1 : 50	$\times 125$
0.4 " " " "	1 : 25	$\times 62.5$
0.5 " " " "	1 : 20	$\times 50$
1.0 " " " "	1 : 10	$\times 25$

#### A. *With Thoma ruling : calculation for leucocytes*

All the leucocytes in the whole of the cross-ruled area are counted; as least four separate counts should be made and the average count taken.

This area of 1 square millimetre represents a cubic capacity of 0.1 cubic millimetre. This when multiplied by 10 gives the number of cells per cubic millimetre of diluted blood and when again multiplied by the diluting factor (10 or 20) the number of per cubic millimetre of whole blood.

Thus, the number of cells multiplied by 100 (when the dilution is 1 : 10) or by 200 (when the dilution is 1 : 20) gives the number of cells per cubic millimetre of undiluted blood.

#### B. *Counting by field method for low counts*

This method is suitable in kala-azar or other diseases in which there is usually a leucopænia. Take blood up to 0.5 mark of the white cell pipette and dilute it 1 in 20.

With  $5 \times$  eyepiece and  $\frac{1}{4}$ th objective focus the square in the centre of the field of the counting chamber with the Thoma ruling, or the centre block of the Neubauer, and draw out the tube until the diameter of the field measures eight times the length of the side of a small square. The area of the *whole field* is now equal to the area of 50 small squares almost exactly ( $\pi r^2 = \frac{2^2}{4} \times 16 = 50.2857$ ).

Count the number of cells in 40 such different fields.

*Calculation.*—The volume of each square is  $1/4,000$  cubic millimetre and each field contains 50 squares.

Thus, if the total number of cells in 40 fields is 70, the number of cells per cubic millimetre

$$\text{of blood} = \frac{4,000 \times 20}{50 \times 40} \times 70 \\ = 2,800$$

The same result may be obtained by multiplying the total number of cells in 40 fields by 40 if the dilution is 1 : 20, or by 20 if the dilution is 1 in 10.

With this method, cells of a very large area are counted and the multiplying factor is only 40, or 20.

#### *Enumeration of the nucleated cells of the marrow*

The enumeration of the nucleated cells of the marrow from the material obtained by sternal biopsy is carried out in the same way as that of the leucocytes in the leukaemic cases.

#### *Care of the instruments*

After use, the pipettes, coverslip and the hæmocytometer must be cleaned thoroughly.

#### *Cleaning the pipettes*

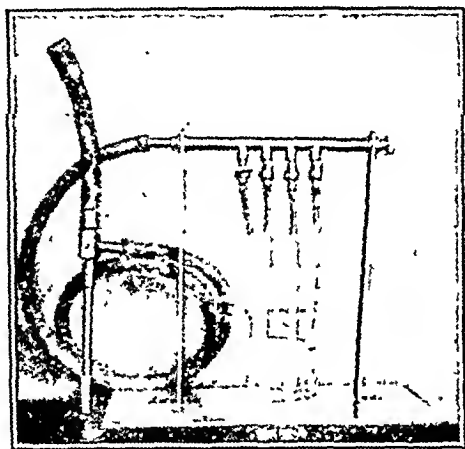
1. Thoroughly wash out all the diluted blood with water.
2. Remove water with absolute alcohol.

3. Remove alcohol with ether.

4. Pass air through to dry the pipette, so that the bead rolls freely in the bulb.

It is a very laborious process to clean the pipettes by blowing through them, further, one cannot dry them properly by blowing, as expired air is laden with moisture. The pipettes can be cleaned easily and dried by attaching them to a suction pump (figure 6), or when this is not available by attaching them to a syringe.

Fig. 6.



Suction pump for cleaning pipettes.

If the cells clog the tip or any part of the capillary tube, loosen them by inserting a stiff horse hair.

If there is albuminous matter in the bulb, fill it up either with saturated solution of NaOH or potassium bichromate cleaning solution, keep overnight in the 37°C. incubator, and clean next morning.

#### *Cleaning counting chamber and coverslip*

Wash the ruled side of the counting chamber and the coverslip in running water. Thoroughly dry, first with a clean cotton handkerchief and finally with a silk handkerchief or selvyt cloth

## HOSPITAL ORGANIZATION WITH SPECIAL REFERENCE TO CONDITIONS IN INDIA

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THE population of British India in 1936 was 281,866,639. The birth-rate and death-rate were 35 per mille and 23 per mille, respectively. The infantile death-rate per 1,000 live births was 162. As against this, in 1937 the birth-rate and death-rate in England and Wales were 14.9 and 12.4 per thousand, respectively, the infantile

or lens paper, but avoid rubbing the ruled area of the counting chamber.

From time to time the counting chamber and the coverslip should be wiped with alcohol or acetone to remove any grease and then dried with the silk handkerchief, but on no account should the counting chamber be immersed or freely cleaned with alcohol.

If the rulings become faint after long use, the lines may be made prominent by lightly rubbing with a silk cloth on which graphite (lead from a pencil) has been rubbed.

#### *Normal standards*

The number of red cells per c.mm. is usually given in textbooks as 5,000,000. This figure is too low for men and too high for women. The mean of a number of counts in different populations is given in the table.

It will be seen that there is a striking uniformity in the counts in different populations, compared for example with the hæmoglobin estimations in the same range of populations.

#### REFERENCE

These were given in part I (*I. M. G.*, February 1940).

*Table showing the normal red cell counts of different populations*

Sex	Age	Locality	Economic status	Number	Mean red cell per c.mm. in millions	Standard deviation	Authority
Males	19-30	Bombay	Students, etc.	121	5.110	± 0.380	Sokhey <i>et al.</i> , 1937.
	25-45	Calcutta	Mixed	50	5.362	± 0.633	Napier and Das Gupta, 1935a.
	20-45	"	"	30	5.533	± 0.490	" " " 1936.
	19-30	Assam	Coolies	24	5.353	± 0.620	" " " 1935b.
	19-30	"	"	20	5.270	± 0.710	" " " 1936.
		Cachar	"	25	5.057	± 0.563	Napier and Majumdar, 1938.
	Adults	U. S. A.	"	..	5.400	..	Castle and Minot, 1936.
	"	Britain	"	..	5.690	..	Whitby and Britton, 1939.
		"	"	..	5.428	..	Price-Jones, 1931.
		"	"	..	4.470	± 0.230	Sokhey <i>et al.</i> , 1938.
Females	16-30	Bombay	Middle class	101	4.615	± 0.409	Napier, 1939.
	14-38	Calcutta	"	125	4.560	± 0.250	Benjamin, 1939.
	17-30	Delhi	Middle class	101	4.454	± 0.705	Napier and Majumdar, 1938.
		Cachar	Coolies	25	4.550	± 0.650	Napier and Bilimoria, 1937.
		Assam	"	20	4.800	..	Whitby and Britton, 1939.
		Britain	"	..	5.012	..	Price-Jones, 1931.
		"	"	..	4.750	..	Bethel, 1936.
	18-22	Michigan	Students	50			

mortality was 58 per 1,000. The average yearly deaths for British India for 1927 to 1936 were 6,326,893. The mean mortality figures from the principal diseases were as follows:—

Small-pox .. ..	82,529
Plague .. ..	52,238
Dysentery and diarrhoea	249,983
Cholera .. ..	222,181
Respiratory diseases ..	426,725
Malaria .. ..	1,506,064 (1934-36)

These figures speak for themselves; there is no need to comment on the conditions prevailing in India. It must not be imagined that conditions have always been satisfactory in Great Britain. In this connection it would be of interest to review the development of the health services in England. *England and Scotland* throughout the Middle Ages and down to the nineteenth century were periodically ravaged by epidemics of plague, cholera and small-pox. During the period of the 'Black Death', it is estimated that about one-third of the population died of the disease. During a part of the eighteenth century one child out of every three under the age of 5 in Glasgow died of small-pox. The conditions began to improve in the nineteenth century.

In a recent paper in the *British Medical Journal* (25th February, 1939) the development of the responsibility of the State for public health in England was described. The first Sanitary Commission to investigate the general condition of the health of the labouring population of Great Britain was appointed and Chadwick was the author of the report which became, and has remained ever since, an authoritative presentation of the medical aspects and needs of the social life of the people. It was followed by a long series of public enquiries and Royal Commissions in which medical men played a prominent part. The result was that the state set up a central health organization (formerly the Local Government Board and now the Ministry of Health), divided the country into sanitary districts, and made each district self-governing, on lines laid down by Parliament with reference to sanitation, water-supply, sewage disposal, housing, nuisances, the suppression of the causes of disease, food inspection, and the correct certification of sickness and death; these legislative measures found expression in the Public Health Act of 1875 and four score of subsequent enactments. It is significant that as these acts succeeded one another, the measures they instituted became more personal, more direct and more medical, so that to-day the public health services administered by local authorities and their numerous medical officers are concerned, not only with the subject of external environment but with health and disease of the individual, *e.g.*, with industrial hygiene, maternity and infant welfare, the school medical service, the provision of the Cleansing of Person Acts, the direct treatment of communal diseases (including fevers,

tuberculosis, venereal diseases, rheumatism, blindness and lunacy), the provision of institutions (clinics, hospitals, sanatoria, and special schools for defective children), a health and unemployment insurance system, medical research, the education of the people in health, international sanitary laws, and the imposition of statutory duties on the medical profession on behalf of preventive medicine. How great has been the expansion is indicated by the official report of the Treasury of the fact that in 1900 the nation spent 31 millions on public social services in England and Wales (education, public health, lunacy, poor relief) whilst in 1932, the sum had risen to 430 millions (including insurance and pensions). Here is a gigantic scheme of national, social, and health enterprises for the welfare of the people, and with this scheme the medical profession is now intimately associated as adviser or agent. If India is to solve her pressing medical and public health problems in a satisfactory manner an organization on similar lines to those in Great Britain, but modified with due regard to conditions in India, will have to be set up in the near future.

One of the most important of the many urgent problems in this connection is the provision of adequate hospital accommodation for the people, which is the only way in which expert medical aid can be administered to the people in case of sickness and debility of a serious nature.

A brief reference to the history of origin of hospitals will not be out of place here. In the early days of the Christian era no establishments were founded in Europe for the relief of the sick till the time of Constantine. The connection between monasteries and hospitals became well established between A.D. 1000 and 1050. The Caliph Harun-al-Rashid (A.D. 736-809)

TABLE I  
Average area and population served by each hospital or dispensary

Province	Total number of hospitals and dispensaries in the province	Average area served by each hospital or dispensary (sq. miles)	Average population served by each hospital or dispensary
Madras ..	1,134	126	41,217
Bombay ..	429	180	41,940
Bengal ..	1,449	540	34,585
United Provinces	597	178	81,087
Punjab ..	896	111	26,318
Central Provinces	343	291	45,212
Bihar ..	528	131	61,310
Delhi ..	24	24	26,510
Baluchistan ..	41	1,327	11,305
Ajmer-Merwara	10	271	56,029

attached a college to every mosque and to that again a hospital. The Buddhists in India had their hospitals as early as 260 B.C.; Hindustan could then boast of many hospitals founded by

TABLE V

*Total number of nurses and midwives employed in the various hospitals of British India*

Province	HOSPITALS WITH IN-PATIENTS			HOSPITALS AND DISPENSARIES WITH OUT-PATIENTS ONLY			Total
	Nurses	Midwives	Male nurses	Nurses	Midwives	Male nurses	
Madras .. ..	1,641	640	73	1	505	38	2,898
Bombay .. ..	1,308	388	111	13	28	7	1,855
Bengal .. ..	860	122	77	5	7	0	1,071
United Provinces ..	439	84	65	4	2	1	595
Punjab .. ..	651	331	47	8	1	0	1,038
Bihar .. ..	300	123	28	0	8	0	459
C. P. and Berar ..	381	110	30	1	12	1	535
Assam .. ..	201	65	16	0	2	0	284
Sind .. ..	106	74	0	3	1	0	184
Orissa .. ..	70	81	9	1	16	19	196
Delhi .. ..	247	20	2	3	0	0	272
N.-W. F. Province ..	56	3	94	0	1	2	156
Baluchistan .. ..	4	9	78	0	0	1	92
Ajmer-Merwara ..	17	4	23	1	0	2	47
Coorg .. ..	0	1	0	0	6	0	7
Central India Agency ..	36	19	2	0	0	0	57
<b>TOTAL ..</b>	<b>6,317</b>	<b>2,074</b>	<b>655</b>	<b>40</b>	<b>589</b>	<b>71</b>	<b>9,746</b>
		<b>9,046</b>			<b>700</b>		

under a financial arrangement made with public authorities, approved societies, employers of labour, insurance companies, and others. The great majority, probably 80 to 85 per cent of all hospital patients, can thus be dealt with and the hospital services can be adequately financed by one or other of these methods. All persons above the agreed income limit should be regarded as private patients and should be prepared to meet the special charges for maintenance and medical services appropriate to that class. Such persons do not normally constitute more than 5 per cent of applicants for hospital service.

A 'clearing house' (i.e., a central bureau) to co-ordinate the distribution of cases requiring admission to the various hospitals and to provide information as to where and when special forms of treatment and other forms of diagnostic help are available, would be desirable under a system of co-ordination of grouped hospitals. It should also co-ordinate the hospital ambulance transport of the area.

In the year 1937, the number of insured persons entitled to the benefit of the Insurance Medical Services in England and Wales was 17,032,000, an increase of 712,000 on that for 1936, while the number of insurance practitioners was 16,800, an increase of 50.

The only way in which India can hope to solve the question of the extreme paucity of the hospital accommodation available for its inhabitants is to develop and finance its hospitals somewhat on the lines on which it is being done in Great Britain and other advanced countries of the world. Now that the old prejudice against hospital treatment is disappearing

rapidly and the people are beginning to understand that when one is really ill there is no place better than the ward of a good hospital, there should be no difficulty about it. The only thing which is militating against the hospitals at the present time is the unsatisfactory manner in which many of these institutions are being run, all over the country. I have no doubt that the development of a contributory scheme for hospital benefit in India will succeed and is in fact the only way in which the hospitals can be made efficient with regard to their personnel, equipment and the required number of beds per thousand of population ensured. The state in this country is already doing a great deal towards supplying the hospital accommodation. It makes large grants-in-aid to private medical institutions, local boards and municipalities. Although the amount is substantial, yet it cannot meet the needs of the country. It is not possible for the state to make more contributions without any increase in taxation. Under the circumstances what should be developed further is the voluntary and municipal hospitals. The local authority provides as many as 124,169 beds in general hospitals in England.

The voluntary hospitals can derive their funds from the following sources:—

(a) Gratuitous contributions, i.e., contributions from whatever source to which no such conditions are attached (either expressly or by implication) as would involve obligation of service on the part of the hospital, but are charitable contributions to be expended at the discretion of those to whom the management of the hospital is entrusted.



(b) Contributions for services rendered, or to be rendered, i.e., contributions for hospital benefit made either by patients themselves or on their behalf by individuals or associations, or, in case of local authorities, payment made for the maintenance and medical treatment of patients for whom these authorities are responsible.

Persons applying for free treatment in such hospital service will have to be certified by the almoner or other officer of the hospital as unable to contribute in any way towards their maintenance and medical treatment. Only then will the hospital benefit be provided by the gratuitous contributions placed at the discretion of the hospital authorities and by the gratuitous services of the visiting medical staffs.

The contributory system has already been introduced in a rudimentary form in many of the provinces in India, though Bengal has not yet taken it up. Poor and indigent patients, both indoor and outdoor, are given free medical and surgical treatment in all provinces in India. They are not charged any fees, nor are they required to pay for any special treatment, or for drugs not ordinarily available at the hospital. Patients whose monthly income does not exceed Rs. 30 p.m. in Madras and Bombay, Rs. 150 in the Punjab, Rs. 100 in Delhi, and with an annual income of less than Rs. 2,000 in the United Provinces and Central Provinces fall into the category of those who are exempted from hospital fees.

In the case of persons employed in factories, mines, quarries, tea estates and railways in Madras, Bombay and Sind, if admitted as in-patients at the instance of their employers, a charge of As. 8 is levied from the employers, but if they attend government hospitals of their own accord they are treated as members of the general public for purposes of hospital charges.

In the Central Provinces and Berar the system of charging a fee of two pice to each new patient, except paupers, attending a hospital or dispensary had been in force since 1933. The amounts received on that account in most cases were insignificant and with a few exceptions there had been an undoubted fall in the out-patients' attendance. It was thought that if the system were conscientiously worked out it was bound to lead to a 'set-back' to the popularity of scientific medicine and the local government therefore allowed its discontinuance in the year 1936.

In the North-West Frontier Province an innovation of interest has been the starting of 'paise' dispensary, where everybody is required to pay one pice for the day's medicine supplied, and the income thus derived goes towards the running expenses of the dispensary. The success of this dispensary has led to the opening of similar ones elsewhere.

India could with advantage copy the system followed by certain countries on the continent of Europe. The plan pursued is to demand

payment from all patients who are admitted to the hospital under a scale of charges divided into three or four grades. The first grade pays a substantial sum and obtains anything or everything the patient may care to have or pay for, subject to the control of the medical attendant. The second pays much less, but a remunerative rate for all they receive at the hospital, and the third and fourth classes are very poor people or paupers, who are paid for on a graduated scale by the municipalities or corporations. The local authorities can levy a medical cess based on the amount of rent paid. Under this system well-to-do thrifty artisans and improvident paupers are all treated by one staff, controlled by one administration, and are located in immediate proximity to each other though in separate pavilions. This plan should be accompanied by a system of health insurance, whereby all classes who desire to be thrifty pay a small annual premium in the days of health, and secure adequate hospital treatment and care when ill. The details of the insurance scheme can be easily worked out by an expert committee. The state can be moved to enact the appropriate laws.

A complaint frequently made against the administration of Indian hospitals is that large numbers of patients who can really afford to pay are treated free of charge. The problem is not simple, because modern scientific medicine is costly, and, although a person may not be indigent as regards the ordinary necessities of life, he is often unable to pay for even minimum requirements when sick. In the absence of an almoner system, hospital abuse is not easy to detect, but is probably less common than is frequently suggested. The increasing employment of honorary medical officers in hospital out-patients departments will probably be a useful corrective, since the final decision as to the patient's eligibility for free treatment rests largely with the doctor.

In order to obtain more funds for the running of hospitals, an almoner system should be instituted in the existing medical institutions. The extension of hospital facilities must depend on a demand from the public. It is for the state to act as a co-ordinating agent between the state, municipal and voluntary hospitals.

## BRITISH PHARMACEUTICAL PRODUCTS

Two lists of pharmaceutical products that are made in the United Kingdom are given below; in the first table are included those products which have essentially the same chemical composition as some well-known drugs of foreign, but not necessarily enemy-country, manufacture. The second table gives the drugs which have a similar therapeutic action to those mentioned in the foreign list. Many of the products included in the foreign list will be available in India and some of the British products may not, on account of the restriction in exports at present in force in Great Britain.

It is not claimed that the list is comprehensive, either in the matter of the drugs mentioned or in the names of the manufacturers.

The star (\*) placed against some of the names of foreign products indicates that these products are now also manufactured in Great Britain.

TABLE I

*Showing foreign products of which there are British products with the same essential composition.*

Foreign product	British product	British maker and/or supplier
Acecoline	Acetylcholine chloride	B. D. H.; B. W.; Evans.
Acidol pepsin	Betaine hydrochloride and pepsin.	Boots; B. D. H.; Evans.
Adalin	Carbromal B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Afenil	Calcium chloride and urea	B. D. H.; Evans.
Agurin	Theobromine and sodium acetate.	Boots; B. D. H.; Evans; M. & B.; Whiffen.
Airol	Bismuth oxyiodogallate	Boots; B. D. H.; B. W.; Evans; M. & B.; Whiffen.
Aluoin	Diamorphine	M. & B.
Alypin	Amydracaine hydrochloride	Evans.
Anæsthesin	Benzocaine B. P.	A. & H.; Boots; B. D. H.; Evans.
* Antiphlogistine (Denver).	Kaolin poultice B. P.	A. & H.; Boots; B. D. H.; Evans.
Aperitol	Phenolphthalein B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Aphrodine	Yohimbine	B. D. H.; Evans.
Argyrol	Silver vitellin	Boots; B. D. H.; Evans; M. & B.
Aristol	Thymol iodide	A. & H.; Boots; B. D. H.; Evans; Howards; M. & B.; Whiffen.
Arrhenal	Disodium methylarsenate	B. D. H.; Evans.
Atocin	Cinchophen B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Atophan	Cinchophen B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Atophan balsam	Ung. agotan co.	Howards.
Atoxyl	Soamin	B. W.
	Sodium arsenilate	Evans; M. & B.
* Aurobin (Richter)	Crisalbine	M. & B.
Bayer 205	Antrypol	B. D. H.
Betaxin	Vitamin B <sub>1</sub>	A. & H.; B. D. H.; B. W.; Evans; Glaxo; M. & B.
	Berin	Glaxo.
Bismogenol	Injection bismuth salicylate B. P.	A. & H.; Boots; B. D. H.; Evans.
Bismosalvan	Quinine iodobismuthate	A. & H.; B. D. H.; Evans; Whiffen.
	Quinostab	Boots.
	Rubyl	M. & B.
Bitæmaine	Benzamine	Boots; B. D. H.; B. W.; Evans.
Bromural	Dormigene	A. & H.
Calcium diuretin	Theobromine calcium salicylate	Boots; Evans; Whiffen.
* Calsoid	Calcium o-iodoxybenzoate	Whiffen.
	Arthrytin	M. & B.
Cantan	Ascorbic acid B. P. (vitamin C).	A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo.
	Celin	Glaxo.
	Planavit C	M. & B.
Cardiazol	Phrenazol	Boots.
Chinosol	Potassium hydroxy-quinoline sulphate.	A. & H.; Boots; B. D. H.; Evans.
	Soloid chinosol	B. W.
Chloretone	Chlorbutol B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Coramine (Ciba)	Anacardone	B. D. H.
	Nicamide	B. W.
Creosotal	Creosote carbonate	Boots; B. D. H.; Evans.
Dermatol	Bismuth subgallate	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Devegan	Acetarsol vaginal compound	Evans.
	Stovarsol vaginal compound	M. & B.
* Dial (Ciba)	Allobarbitone	A. & H.; Boots; B. D. H.; Evans.
Digitaline Nativelle	Digitalin granules	A. & H.; Boots; B. D. H.; Evans.
	Digitoxin	Boots.
	Tabloid digitalin cryst	B. W.
Dionin	Ethylmorphine hydrochloride	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Diuretin	Theobromide and sodium salicylate B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.; Whiffen.
	Guaiacol carbonate	A. & H.; B. D. H.; B. W.; Evans; M. & B.
Duotal	Benzyl succinate	A. & H.; B. D. H.; Evans.
Esterol	Pyrogallol monoacetate	B. D. H.; Evans.
Eugallol	Tabloid ophthalmic euphthalmine hydrochloride.	B. W.
Euphthalmine		

TABLE I—*contd.*

Foreign product	British product	British maker and/or supplier
Euquinine	Quinine ethyl carbonate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Euresol	Resorcin monoacetate	A. & H.; Boots; B. D. H.; Evans.
Exalgin	Methylacetanilide	A. & H.; Boots; B. D. H.; Evans.
Ferronyl	Citrated ferrous chloride B. P.	A. & H.; B. D. H.; B. W.; Evans; Howards.
Fibrolysin	Thyosinamine sodium salicylate.	Boots; B. D. H.; Evans.
Germanin	Antrypol	B. D. H.
Helmitol	Formamol	A. & H.; B. D. H.; Evans.
Hydropyrin	Lithium acetyl-salicylate	A. & H.; Boots; B. D. H.; Evans; Howards.
Hypophysin	Pituitary extract B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo.
Ichthyol	Ichthammol B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Iod-calcium diuretin	Potassium iodide and theobromine calcium salicylate.	Whiffen.
Iodeikon	Iodophthalein B. P.	A. & H.; B. D. H.; Evans.
	Stipolac	B. W.
	Opacol. opacin	M. & B.
Iodipin	Iodized oil B. P.	A. & H.; Evans.
	Iodatol	B. D. H.
	Neo-hydriol	M. & B.
Iod-tetragnost	Iodophthalein B. P.	A. & H.; B. D. H.; Evans.
	Stipolac	B. W.
	Opacol. opacin	M. & B.
* Kalmopyrin (Richter)	Calcium acetyl-salicylate	A. & H.; Boots; B. D. H.; Evans; Howards.
* Larostidine (Roche)	Histidine	A. & H.; B. D. H.; B. W.; Evans.
	Stellidin	M. & B.
Lenigallol	Pyrogallol tri-acetate	B. D. H.; Evans.
Lipiodol	Oleum iodisatum B. P.	A. & H.; Boots; B. D. H.; Evans.
	Neo-hydriol	M. & B.
	Iodatol (iodized oil 40%)	B. D. H.
Luminal	Phenobarbitone B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
	Gardenal	M. & B.
	Tabloid phenobarbitone	B. W.
Luminal sodium	Soluble phenobarbitone B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
	Gardenal sodium	M. & B.
	Tabloid soluble phenobarbitone	B. W.
Magnesium perhydrol	Magnesium peroxide	A. & H.; Boots; B. D. H.; Evans; M. & B.
Medinal	Soluble barbitone B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
	Tabloid soluble barbitone	B. W.
Migrainin	Phenazone caffeine citrate	A. & H.; Boots; B. D. H.; Evans; M. & B.
Myosalvarsan	Sulpharsphenamine B. P.	Boots; B. W.; Evans; M. & B.
	Sulphostab	Boots.
	Kharsulphan	B. W.
	M. A. B.	M. & B.
Naganol	Antrypol	B. D. H.
Neocaine	Procaine hydrochloride B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
	Arecan	Evans.
	Planocaine	M. & B.
Neohydropyrin	Magnesium acetyl-salicylate	B. D. H.; Evans.
	Magsyn	A. & H.
Neosalvarsan	Neosarsphenamine B. P.	A. & H.; Boots; B. W.; Evans; M. & B.
	Novarsan	A. & H.
	Novostab	Boots.
	Neokharsivan	B. W.
	N. A. B.	M. & B.
Neo-trepol	Injection bismuth B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
	Bismostab	Boots.
	Hypoloid bismuth metal	B. W.
	Bisglucol	M. & B.
Novocain	Procaine hydrochloride B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
	Planocaine	M. & B.
* Omnopon (Roche)	Papaveretum	B. D. H.; Evans.
	Alopon	A. & H.
Orthoform	Orthocaine B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Panflavin tablets	Planacrine	M. & B.
Pantopon	Papaveretum	B. D. H.; Evans.
	Alopon	A. & H.
Parathormone	Parathyroid extract	Evans.
	Euparatone	A. & H.
Pentnucleotide	Pentide	A. & H.
	S. P. N. Evans	Evans.
Perhydrol	Hydrogen peroxide 100 vols.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Petein	Whooping-cough vaccine	B. D. H.; B. W.; Evans; Glaxo.

TABLE I—concl'd.

Foreign product	British product	British maker and/or supplier
Progynon	Ovostab Oestroform Oestrinum	Boots. B. D. H. Evans.
Prolan	Physostab Antostab Gonan	Boots. Boots. B. D. H.
Proluton	Luteostab	Boots.
Prontosil album	Progestin B. D. H. Sulphanilamide Streptocide	B. D. H. A. & H.; Boots; B. D. H.; B. W.; Glaxo; M. & B. Evans.
Protargol	Silverproteinat B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Pyoktanin violet	Methyl violet	A. & H.; Boots; B. D. H.; Evans.
Pyoktanin yellow	Auramine	B. D. H.
Pyramidon	Amidopyrine B. P. Tabloid amidopyrine	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B. B. W.
Pyramidon salicylate	Amidopyrine salicylate	A. & H.; B. D. H.; Evans; M. & B.
Salipyrin	Phenazone salicylate	A. & H.; B. D. H.; Evans.
Salit	Bornyl salicylate	
Salyrgan	Injection mersalyl B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans.
Sanocrysin	Crisalbine	M. & B.
Selvarol	Calcium gluconate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards; M. & B.
Sionon	Sorbitol	A. & H.; B. D. H.; Howards; M. & B.
Spirobismol	Quinine iodobismuthate Quinostab Rubyl	A. & H.; B. D. H.; Evans; Whiffen. Boots. M. & B.
Spirocid	Acetarsol B. P. Orarsan Kharophen Stovarsol	Evans. Boots. B. W. M. & B.
Stypticin	Cotarnine hydrochloride	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Styptol	Cotarnine phthalate	A. & H.; Boots; B. D. H.; Evans; M. & B.
Styracol	Guaiacol cinnamate	B. D. H.; Evans; M. & B.
* Sulfarsenol	Sulpharsphenamine B. P. Sulphostab Kharsulphan M. A. B.	Boots; B. W.; Evans; M. & B. Boots. B. W. M. & B.
Superol	Potassium hydroxy quinoline sulphate.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Suprarenin	Soloid chinosol	B. W.
Tannalbin	Adenaline B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Tannigen	Albumin tannate	A. & H.; B. D. H.; Evans; M. & B.
Tannoform	Acetannin	A. & H.; B. D. H.; Evans; M. & B.
Theocin sodium acetate	Methylene ditannin Theophylline and sodium acetate B. P.	B. D. H.; Evans; M. & B. Boots; B. D. H.; Evans; M. & B.
Theominal	Theobromine and phenobarbitone B. P.	A. & H.; Boots; B. D. H.; Evans.
Thiocol	Theogardenal	M. & B.
Tiodine	Potassium guaiacol sulphonate Thiosinamine ethyl iodide	A. & H.; B. D. H.; Evans. Boots; B. D. H.; Evans; Glaxo; M. & B.
Trikresol	Iodolysin	A. & H.
Trional	Cresol B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Uden	Methylsulphonal B. P. Oestroform	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B. B. D. H.
Urotropin	Ovostab	Boots.
Varicophytin	Hexamine B. P. Hypertonic solution sodium chloride with anæsthetic.	A. & H.; Boots; B. D. H.; B. W.; Evans. B. D. H.; Evans.
* Veganin (Warner)	Aspirin, phenacetin and codeine phosphate.	A. & H.; Boots; B. D. H.; Evans; M. & B.
Veronal	Barbitone B. P. Tabloid barbitone	A. & H.; Boots; B. D. H.; Evans; M. & B. B. W.
Veronal sodium	Soluble barbitone B. P. Tabloid soluble barbitone	Boots; B. D. H.; Evans; M. & B. B. W.
Vigantol	Liq. calciferol B. P. Viosterol	A. & H.; Boots; B. D. H.; Evans; Glaxo. A. & H.
Xeroform	Radiostol solution and pellets Ostelin	B. D. H. Glaxo.
Yatren	Bismuth tribromphenate	A. & H.; Boots; B. D. H.; Evans; Howards; M. & B.; Whiffen.
Zinc perhydrol	Chiniofon B. P. Quinoxyl Quinosulphan Zinc peroxide	B. D. H.; Evans. B. W. M. & B. B. D. H.; Evans.

TABLE II

*Showing foreign products of which there are British products that have the same therapeutic properties*

Foreign product	British product	British maker and/or supplier
Albargin	Silverproteinate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Algodorm	Barbitone and amidopyrine tablets B. P. C.	A. & H.; Boots; B. D. H.; Evans.
Allochrysine	Myocrisin	M. & B.
Antileprol	Moogrol. Iodized moogrol. Alepol. Ethyl chaulmoograte Ethyl esters of hydnocarpus oil B. P.	B. W. B. D. H. B. D. H.; Evans.
Arcanol	Cincophen and aspirin	Boots; B. D. H.; Evans.
Aristochin	Quinine ethyl carbonate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans.
Arrhenal	Soamin	B. W.
Arsen-triferrin	Iron and arsenic ampoules and/or tablets.	A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo.
Aspiphenin	Aspirin and phenacetin	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Asthmolysin	Pituitary extract and adrenaline.	A. & H.; Boots; B. D. H.; Evans.
Atophan balsam	Analgesic balm Analgesic cream (vanishing) Regesan pain relieving balm Menthofax	Evans. B. D. H. Boots. B. W.
Atophanyl	Cinchophen and sodium salicylate.	Boots; B. D. H.; Evans.
Bioferrol	Hepol with iron Livron Heprona. Hepatex with iron	A. & H. Boots. Evans.
Bismarsen	Biarsamide. Bistovol	M. & B.
Bismogenol	Bisantol	M. & B.
Bivatol	Stabismol Neo-cardyl	Boots. M. & B.
Bromural	Carbromal B. P.	Boots; B. D. H.; Evans; M. & B.
Cafaspin	Aspirin and caffeine	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Calcimint	Calsolact Calsimil Salpern Kalsolac	A. & H. B. D. H. Boots. Evans.
Calcium diuretin	Ostocalcium	Glaxo.
Calcium (Sandoz)	Theobromine and sodium salicylate B. P. Calcium gluconate B. P. Percalcin.	A. & H.; Boots; B. D. H.; Evans; M. & B.; Whiffen. A. & H.; Boots; B. D. H.; Evans; Howards; M. & B. Evans.
Calsiod	Levu-calcin (calcium laevulinate) ampoules.	Glaxo.
Campolon	Calcium acetyl-salicylate Hepol. Anaphepol. Azoule liver extract. Hepastab. Hepastab No. 2 Anhæmin. Liver extract (intramuscular injection). Hepatex comp. H. C. I.	Boots; B. D. H. A. & H. Boots. B. D. H.
Carboserin	Examen	Evans Glaxo.
Cardiazol	Activated carbon Charcoal and kaolin Anacardone	A. & H.; Boots; B. D. H.; Evans. Boots; Evans. B. D. H.
Casbis	Nicamide } For use as Cardatone } cardiac Dacorene } stimulant.	B. W. Evans M. & B.
	Injection bismuth salicylate B. P.	A. & H.; B. D. H.; Evans.
	Stabismol Neo-cardyl	Boots. M. & B.
Cignolin	Bisantol	M. & B.
Cito-baryum	Chrysarobin B. P. Barium meal Novumbrose. Umbrose Shadofom Barolac Fotonemal. Fotamealo. Fotamilk.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B. Boots; Glaxo A. & H. B. D. H. B. W. Evans.
Codeonal	Soluble barbitone and codeine	Boots; B. D. H.; Evans.
Compral	Amidopyrine B. P.	Boots; B. D. H.; B. W.; Evans.

TABLE II—*contd.*

Foreign product	British product	British maker and/or supplier
Coramine (Ciba)	Cardatone	Evans.
Cryogenine	Dacorene	M. & B.
Cycloform	Phenylsemicarbazide	B. D. H.; Evans; M. & B.
Cycloform ointment	Benzocaine B. P.	A. & H.; Boots; B. D. H.; Evans.
	Benzocaine, extract of hæmamelis and zinc oxide ointment.	B. D. H.
	Ung. hæmamelis co. Evans	Evans.
Cylotropin	Hexamine, sodium salicylate, and caffeine.	B. D. H.; Evans.
Digipuratum	Digitalin granules	A. & H.; Boots; B. D. H.; Evans.
	Tab. digitalis leaf B. P.	A. & H.; Boots; B. D. H.; Evans.
	Diginutin. Digoxin	B. W.
Digitaline Nativelle	Tabloid digoxin	B. W.
Dijodyl	Iodoprotein	Boots.
	Iodicin	B. W.
	Iodocasein	Whiffen.
Eldoform	Albumin tannate	B. D. H.; Evans; M. & B.
Elityran	Thyroxine sodium B. P.	Boots; B. D. H.; B. W.; Evans.
	Thyroid B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans.
	Tabloid thyroxine	B. W.
Elixir Gabail	Elixir bromovalerianate	Boots; Evans.
	Euvalerol B	A. & H.
	Elixir valibrom B. D. H.	B. D. H.
Ephetonin	Ephedrine hydrochloride	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Esmodil	Acetylcholine	B. D. H.; Evans.
	Hypoloid acetylcholine bromide.	B. W.
	Pragmoline	M. & B.
Euphthalmine	Atropine sulphate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Whiffen.
	Homatropine hydrobromide	A. & H.; Boots; B. D. H.; B. W.; Evans.
Fæxalin } Fæxin } Femergin }	Dried brewer's yeast	A. & H.; Boots; B. D. H.; Evans.
	Ergotoxine ethane sulphonate B. P.	B. D. H.; B. W.; Evans; M. & B.
Ferronyl	Ferosan	Boots.
	Fersolate	Glaxo.
Fibrolysin	Iodolysin	A. & H.
	Thiosinamine ethyl iodide	Boots; B. D. H.; Evans; Glaxo.
Gonosan	Sandalwood oil and kava-kava resin.	B. D. H.; Evans.
	Kavol	A. & H.
	Savaresse's santal	Evans.
Gravitol	Ergotoxin ethane sulphonate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo.
	Ergometrine B. P.	A. & H.; B. D. H.; B. W.; Evans; M. & B.
	Erbolin	Glaxo.
	Ernutin	B. W.
Hegonon	Silver proteinate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Helmitol	Cystazol	A. & H.
Hepatopson liq.	Liquid extract of liver B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans.
	Hepol	A. & H.
	Hepatex	Evans.
	Compound extract of liver	Boots.
Hexal	Hexamine B. P.	A. & H.; Boots; B. W.; B. D. H.; Evans; M. & B.
Hexophan	Cinchophen B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards;
		M. & B.
Hypertherman	T. A. B. vaccine B. P.	B. D. H.; B. W.; Evans; Glaxo.
	Normal horse serum	A. & H.; B. W.; Evans.
Ichthalbin	Ichthammol B. P.	A. & H.; Boots; B. D. H.; Evans.
Impletol	Procaine hydrochloride and caffeine.	B. D. H.
	Arecan spinal anæsthetic	Evans.
Inkretan	Thyroid and pituitary	Boots; B. D. H.
	Thyroxex	Evans.
Iod-calcium-diuretin	Potassium iodide and theobromine sodium salicylate.	Boots; B. D. H.; Evans; Whiffen.
Iodival	Iodoprotein	Boots.
	Iodocasein	Whiffen.
Juvenin	Yohimbine, nuxvomica and damiana pills.	B. D. H.
	Damiana pills	Evans.
Keraphen	Iodophthalein B. P.	A. & H.; B. D. H.; Evans.
	Stipolac	B. W.
	Opacol. Opacin	M. & B.



TABLE II—*contd.*

Foreign product	British product	British maker and/or supplier
Krysolgan	Crisalbine. Myocrisin	M. & B.
Lacarnol	Adenosine	B. D. H.
Lopion	Crisalbine. Myocrisin	M. & B.
Mapharsen	Neorarsphenamine B. P.	Boots; B. W.; Evans; M. & B.
	Novostab	Boots.
	Neokharsivan	B. W.
	Halarsol. N. A. B.	M. & B.
Matronax	Ovary and thyroid	Boots; B. D. H.; Evans.
	Thyro-varium	B. W.
Neo-oleosal	Injection bismuth salicylate	A. & H.; B. D. H.; Evans.
	B. P.	
	Stabismol	Boots.
	Neo-cardyl	M. & B.
Neo-reargon	Silver proteinate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
	Soloid silver proteinate	B. W.
Neostibosan	Neostam	B. W.
Neutralon	Magnesium trisilicate	A. & H.; Boots; B. D. H.; M. & B.
	Colloidal kaolin	B. D. H.; Evans.
	Osmo-kaolin	A. & H.
	Collumina. Novasorb	Evans.
Noctal	Phenobarbitone B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.
	Gardenal	M. & B.
	Tabloid phenobarbitone	B. W.
	Soneryl	M. & B.
Novalgin	Amidopyrine B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans.
	Sonalgin	M. & B.
	Amidopyrine salicylate	B. D. H.; Evans.
Novasurol	Injection mersalyl B. P.	A. & H.; Boots; B. D. H.; Evans.
	Neptal	M. & B.
Novatophan	Cinchophen B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards; M. & B.
		Evans.
Novocain	Arecan	B. D. H.; B. W.; Evans; Glaxo.
Omnadin	T. A. B. vaccine B. P.	A. & H.; B. W.; Evans.
	Normal horse serum	A. & H.; Boots; B. D. H.; B. W.; Evans.
Pandigal	Digitalin	B. W.
	Digoxin	A. & H.; Boots; B. D. H.; Evans; M. & B.
Panflavin	Euflavine	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Pantocain	Procaine hydrochloride B. P.	B. D. H.
	Beta-borocaine	Evans.
	Arecan anaesthetics	M. & B.
	Planocaine	A. & H.; Boots; B. D. H.; Evans; M. & B.
Pellidol	Scarlet red ointment	Boots; B. D. H.; Evans.
Phanodorm	Allobarbitone	M. & B.
	Soneryl	A. & H.; Boots; B. D. H.; Glaxo.
Progynon	Stilbestrol	Glaxo.
	Clinestrol	Evans.
Prolan	Ext. pituitary anterior lobe	A. & H.; Evans.
Proluton	Corpus luteum	A. & H.; Boots; B. D. H.; Evans.
Prominal	Phenobarbitone B. P.	Glaxo.
	Solantoin (for epilepsy)	M. & B.
	Rutonal	B. W.
	Tabloid phenobarbitone	Boots; B. D. H.; Evans; M. & B.
Promonta	Casein glycerophosphate	A. & H.
	Bynogen	Evans.
	Lecigen	Gen.
	Sanatogen	Glaxo.
	Farex	M. & B.
Prontosil album	Proseptasine M. & B. 693	A. & H.; Boots; B. D. H.; B. W.; Glaxo; M. & B.
Prontosil rubrum	Sulphanilamide	Evans.
	Streptocide	M. & B.
	Proseptasine M. & B. 693	M. & B.
Prontosil soluble	Soluseptasine	Evans.
	Streptocide solution	Boots; B. D. H.; Evans.
Quadronal	Antipyrine, phenacetin, and	
	caffeine.	
Quadronox	Antipyrine, phenacetin, and	B. D. H.; Evans.
	barbitone.	
Recedrin	Ephedrine hydrochloride B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Sajodin	Iodoprotein	Boots.
	Iodicin	B. W.
	Iodocasein	Whiffen.
Salyrgan	Neptal	M. & B.
SantyI	Sandalwood oil capsules	A. & H.; Boots; B. D. H.; B. W.; Evans
	Savaresse's santal capsules	Evans.

TABLE II—concl'd.

Foreign product	British product	British maker and/or supplier
Selvarol	Calcium lactobionate Calcium lævulinate (lævulate) Percalcin Levu-calcin (calcium lævulinate).	A. & H. B. D. H.; B. W.; Evans. Evans. Glaxo.
Solargentum	Silver-protein B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.
Solganal	Crisalbinc	M. & B.
Solganal B	Myocrisin (aqueous)	M. & B.
Solganal B oleosum	Myocrisin (oily)	M. & B.
Spinocain	Procaine, strychnine sulphate and alcohol. Arecan spinalanæsthetic Duracaine (procaine formula P. G.).	B. D. H. Evans. M. & B.
Spirocid	Leucarsone	M. & B.
Thiocol syrup	Bronchial syrup Evans	Evans.
Thyraden	Thyroid B. P. Thyroxine sodium B. P. Tabloid thyroid	A. & H.; Boots; B. D. H.; B. W.; Evans. Boots; B. D. H.; B. W.; Evans. B. W.
Tutocain	Procaine hydrochloride B. P. Planocaine	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B. M. & B.
Uleron	Arecan Sulphanilamide	Evans. A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo; M. & B.
Unden	Streptocide M. & B. 693	Evans; M. & B.
Valisan	Stilbæstrol Clinestrol	A. & H.; Boots; B. D. H.; Glaxo. Glaxo.
Valyl	Bornylisovalerianate	B. D. H.; Evans.
Varicophytin	Menthyl valerianate Bornylisovalerianate Sodium morrhuate Sodium salicylate B. P. Quinine and urethane Hypoloid sodium salicylate Varixol Ethamolin Varicaine	A. & H.; B. D. H.; Evans; M. & B. B. D. H.; Evans. A. & H.; B. D. H.; B. W.; Evans; Glaxo. Boots; B. D. H.; Evans. Boots; B. D. H. B. W. Evans. Glaxo.
Veramon	Barbitone and amidopyrine Sonalgin	M. & B. A. & H.; Boots; B. D. H.; Evans. M. & B.

*Abbreviations.—*

B. D. H. = British Drug Houses Ltd.  
B. W. = Burroughs, Wellcome & Co.  
A. & H. = Allen and Handburys, Ltd.  
Gen. = Genatosan, Ltd.  
M. & B. = May and Baker, Ltd.

Boots = Boots Pure Drug Co., Ltd.  
Evans = Evans Sons Lescher and Webb, Ltd.  
Whiffen = Whiffen and Sons, Ltd.  
Howards = Howards and Sons, Ltd.  
Glaxo = Glaxo Laboratories, Ltd.

## Medical News

### ASSOCIATION OF SURGEONS OF INDIA

THE Association of Surgeons of India offers an annual prize of the value of Rs. 100 to the best essay based on original work on a subject to be decided by the Governing Body of the Association and announced at the beginning of every year.

The following are the conditions of the award:—

1. The competition is open to all qualified medical practitioners registered in India, who have been in practice for not more than 10 years after qualification.  
2. The essay should be based on original work and should be written in English.

3. It should be type-written on one side of the paper only and should not contain the name or other indication of the identity of the competitor.

4. The name, address and qualifications, however, should be written on a separate sheet of paper and enclosed with the essay.

5. The subject for 1940 is 'Blood changes in surgical inflammations'. Candidates may, however, restrict themselves to any one aspect of the subject, and the

essay should reach the Secretary before the 1st December, 1940.

6. The copyright for the winning essay will remain with the Association of Surgeons of India. Other essays will be returned to the senders if accompanied by stamped addressed envelopes.

7. The Governing Body may at its discretion withhold the prize during any year if the essays submitted do not come up to the standard.

8. All communications regarding the above are to be addressed to the Secretary, Association of Surgeons of India, Binfield, Kilpauk, Madras.

### KEEPING YELLOW FEVER OUT OF INDIA

NEW rules designed to keep out yellow fever from India have lately been promulgated by the Government of India for the control of aircraft coming to India from areas in Africa infected with yellow fever.

Henceforth no aircraft which is coming from or on its journey to India, has alighted in Angola, Anglo-Egyptian Sudan south of Khartoum, Belgian Congo,

Cameroons, Dahomey, French Equatorial Africa, French Guinea, French West Africa, Gambia, Gold Coast Colony, Ivory Coast, Kenya Colony, Liberia, Nigeria, Senegal, Sierra Leone, Tanganyika Territory, Togoland, Uganda and Upper Volta Territory will be allowed to land for the first time in British India at any aerodrome other than the Karachi Air Port or the Karachi Marine Air Port.

It will also be an offence for any one to bring into India an aircraft which has on board a case of yellow fever or any person who within nine days of arrival in India has been in an infected area unless he has been protected by satisfactory inoculation or by a previous attack of the disease or has only alighted in an infected area at a non-infected anti-amaryl aerodrome. An aircraft which had on board a case of yellow fever must also have been properly disinfected and appropriate preventive measures must have been taken with regard to the passengers, crew and cargo on board before it can be allowed into India. It will also be an offence for anyone to bring into India an aircraft which has started from or alighted in an infected area and subsequent to such starting or alighting has not obtained from the appropriate authorities a certificate of disinfection. Severe penalties can be imposed on persons who transgress these rules.

Any aircraft which does not satisfy these conditions and attempts to enter into British India may be refused entry.

Should an infected aircraft reach India, both the aeroplane and its cargo will immediately be disinfected. Any persons suffering from yellow fever and any persons who may have been exposed to infection within the previous nine days will be immediately isolated in the mosquito-proof isolation hospital at Karachi.

The rapid development in air traffic in recent years makes it necessary to adopt stringent precautions against the introduction of yellow fever into India. Careful investigations have shown that a large endemic area exists in Africa and the infection is to be found over a much wider tract than was imagined. It has been proved by means of blood tests that yellow fever infection is widely distributed in a region to the south of the Sahara Desert and extending from the coast of Senegal eastwards for over 3,000 miles to the upper region of the Nile in the Anglo-Egyptian Sudan.

*Proximity to infected areas.*—Certain air lines are now carrying passengers and mails *via* Alexandria to the Far East. Another air route is in operation between South Africa and Europe *via* Kenya, Sudan and Alexandria. The latter route traverses areas dangerously near infected parts of Central Africa and actually

passes through certain territories where blood tests have shown that yellow fever has been in existence at least within recent years.

There is also an air route between Lagos in West Africa and Khartoum from and through a territory known to be endemically infected with yellow fever so that it is possible for yellow fever infected persons to be carried to India from these regions within the incubation period of the disease. Moreover, if infected mosquitoes get into an aircraft and bite a passenger en route, that passenger may reach this country in an apparently fit state of health and develop the disease only after his arrival.

Nearly a dozen species of mosquitoes are known to be capable of carrying the disease, but the main culprit is the *Aedes aegypti*, a domestic species of mosquito widely prevalent in India. There is also in India a vast reservoir of monkeys now known to be susceptible to the disease should it become imported into India. The potentiality of real danger is, therefore, apparent.

*Air port of entry.*—Karachi, the converging point of five air lines including all aircraft coming from the West, is the port of entry into India. Being thus in a key position for any preventive campaign against yellow fever, its air port has been provided with a suitable health staff and steps have been taken to prevent the introduction of this scourge. Adequate provision has been made for the segregation of suspected or infected persons arriving by air, a twelve-bedded mosquito-proof hospital having been built on the outskirts of the aerodrome. A mosquito-proof ambulance is also available for transport to hospital of suspected persons arriving at the Marine Air Port.

The fumigation of all aircraft coming from suspected or infected areas has been the general practice for the last two or three years. Every compartment of the aircraft is fumigated before any unloading of baggage, mails, etc., is allowed, so that mosquitoes, if there be any, may be destroyed.

In 1936, the Government of India issued regulations prohibiting entry of aeroplanes which started from or alighted in an infected or suspected area within the previous nine days, unless the person in charge of the aeroplane had, subsequent to such starting or alighting, obtained from the appropriate authorities a certificate of disinfection. The same rule applied to any person who started from or alighted in an infected or suspected area except at an anti-amaryl aerodrome within the previous nine days unless he had been protected by satisfactory inoculation or by a previous attack of the disease. The present rules are an amplification of these regulations.

## Current Topics

### Oxygen Therapy in Pneumonia

By M. A. BLANKENHORN, M.D.

(Abstracted from the *Journal of the American Medical Association*, 7th October, 1939, p. 1410)

CYANOSIS is the main and only important indication for oxygen therapy in pneumonia. While it can be said in theory that cyanosis exists in some degree in every patient with pneumonia, it does not follow that oxygen is always indicated nor is there any justification for the routine use of oxygen to prevent cyanosis.

Cyanosis is a difficult sign to evaluate quantitatively and, since that is exactly what must be done to decide about oxygen therapy, there is a tendency to use it needlessly. This tendency becomes very pressing when the prognosis looks bad and there is not very much to be done about it. Now that there is at hand for most

pneumococcal pneumonia a good remedy, the need for oxygen is definitely reduced. I find in our hospital at Cincinnati that more of our patients have got well and that we have used much less oxygen since we began the use of serum or sulphapyridine in the early stages of pneumonia.

The exact therapy of pneumonia with oxygen has been developed by keeping patients in oxygen-filled rooms for continuous treatment, which treatment is tested by measuring the actual oxygen content of arterial and venous blood. With this experience some of the guesswork goes out and it can be seen that severe anoxemia does occasionally occur in the early stages of pneumonia, oftener in the late stages, and that oxygen sometimes relieves this anoxemia. Severe anoxemia is most likely to occur when many lobes are consolidated; when the respirations become rapid and shallow, *i.e.*, above forty per minute; when there is

moisture in much of the bronchial tree, and when there is wheezing. These circumstances can bring on serious oxygen want which may initiate many symptoms that resemble the toxic effects of infection, viz, steadily rising pulse rate with finally falling diastolic blood pressure, headache, dimness of vision, mental disturbances such as delirium, and coma. Oxygen want may cause or increase abdominal distention, also vomiting. When oxygen is successfully given, many, sometimes all, of the distressing signs and symptoms disappear in a few hours and the treatment then is life saving.

Oxygen treatment may not be successful in relieving anoxæmia for a number of reasons other than reasons of technique. It cannot succeed if too much lung is consolidated or obstructed by exudate. It cannot succeed if the circulation is failing or if there is toxic depression of the respiratory centre by infection or drugs. Since none of these causes of failure are easily apprehended, the technique of administration of oxygen must be carefully ordered and practised by the physician to avoid failure that can be avoided. Important points are these: The supply to the patient must be continuous and abundant, so that only large cylinders are satisfactory; these must be equipped with reducing valves to assure steady flow and flow meters are very useful as well; the inhalation device must be comfortable and must not hamper the free escape of carbon dioxide and moisture. Tents, face masks and nasal tubes can all be made to serve satisfactorily, but they all require skilful and understanding care such as is rarely given by nurses or attendants. They all must be supervised by the doctor, who understands both the disease and the treatment.

Tents are the most expensive, troublesome and difficult to operate but are the most successful generally, except of course the oxygen chamber. Tents are best run by experts, such as the anæsthesia department or gas therapy service in large hospitals. I have found that hospital assistant residents do the job very well in the Cincinnati General Hospital and that they learn a lot about the physiology of respiration by doing that service. Some tents require a gas washer of soda lime to take out the carbon dioxide. This greatly adds to the cost and trouble. Other tents rely on cooling and drying the circulating air with large ice chambers, and much ice is needed for air-conditioning. This cooling and drying to take out carbon dioxide often contributes much to the comfort of the patient. Tents should usually have from 35 to 40 per cent oxygen but may be run for a long time at 60 per cent oxygen. Tents provide a high concentration of oxygen as well as a cool, dry atmosphere, which many patients enjoy if the tent is right. A hot tent, not properly cooled and cleared of carbon dioxide, is a terrible thing to a conscious patient; but there is no need for a tent ever to be uncomfortable. A gas tester is necessary to keep tent service up to this standard. Delirious patients sometimes fight the tent and win, for tents are not tough. In this circumstance the doctor must do some skilful guessing to decide about restraining the fighter or narcotizing him. The first procedure runs up the oxygen need possibly more than it will be helped by the tent; the latter choice depresses the respiration, sometimes increasing the cyanosis. The doctor must keep his eye on cyanosis and try the various chances.

Face masks and face tents in my hands are almost as bad as tents in arousing the fight in a delirious patient. Nasal tubes or catheters are the best for this patient usually.

Face masks are not suited to continuous use, such as the pneumonia patient needs, if the mask is closed. If the device is open to allow unhampered flow of expired air, it becomes a face tent of sorts and I think that with care to details, especially adequate oxygen flow, this arrangement will work; but I have had no real satisfaction in their use. The purpose of such a device is to retain a rich atmosphere during expiration so that when inspiration comes the inrush of room air through the mouth or nose will not dilute the stored gas too greatly.

Nasal catheters are used in many instances, even when tents are at hand. Such an arrangement is simple and costs little, but large cylinders with flow metres are needed as for tents. Catheters are sometimes tolerated by delirious patients who fight the tent. Success of nasal catheters depends on care in placing the catheter tip and keeping it there. The catheter becomes a discomfort for several causes, mostly preventable. If the catheter wiggles about with head motion or bed motion, this is overcome by holding it down to the face with adhesive tape. If the inflow is too fast through a single perforation in the catheter wall, a 'hot spot' develops; this is overcome by moving it about and by humidifying the gas; also by having plenty of openings. Catheters may fail to deliver enough gas if the tip is not near the pharynx. In this circumstance the soft palate may obstruct the inflow and the gas then goes in one nostril and out the other. If the patient breathes through the mouth and the method of inspiration is quick, the inrush of room air dilutes the gas and the whole result is a weak mixture. I know of no way to overcome this difficulty entirely if the patient will not tolerate having his mouth closed with a piece of moist gauze taped over the mouth for a flutter valve. When the catheter tip is well in the oropharynx so that the entire oropharynx is entirely filled with oxygen, this dilution effect is diminished. The dilution effect is also less when the volume of each breath is not great; hence the catheter flow can supply the entire inspiratory volume and even more in rapid and shallow breathing. In some circumstances 40 per cent of oxygen or more has been provided in respired air through the catheter. The catheter should be replaced by a clean one every twelve hours or less. It should be greased with oil that will not evaporate, as with liquid petrolatum, and the nasopharynx sprayed with oil. This protects the mucous membranes from the drying effect that eventually burns or smartens painfully, causing the 'hot spot'. With nasal catheters the oxygen dosage must be regulated with the flow meter; but no one can prescribe the litres per minute that will relieve cyanosis. A good practice is to start the flow at as high a figure as the patient will endure, and 10 litres is about the maximum. If this is adequate, the colour may improve in a few minutes. When there is a definite change, the flow may be reduced; from 6 to 8 litres per minute will generally be tolerated and the cost at this rate of flow is not great. If 10 litres per minute does not help the colour of the patient in an hour, one should try placing the catheter tip lower into the oropharynx—at a spot below the palate but where the swallowing reflex will not interfere. Two catheters, one in each nostril, may be used if the patient breathes through the mouth: the flow to each catheter can then be reduced to a tolerable rate.

Oxygen therapy to be useful must be continuous as long as cyanosis develops if the treatment stops. It is not harmful to stop it for a test of doing without it, except in widespread pneumonia when there is much moisture in the air passages. Here oxygen is helpful and very necessary. Some patients seem to become habituated to a rich atmosphere of oxygen, but this condition does not develop in a short time nor has it been described in lobar pneumonia.

With the best of technique oxygen may in certain cases be life saving to the pneumonia patient, but it is very difficult to prove the point. Where oxygen has been most intelligently used and checked with blood measurements, this form of pneumonia therapy is always regarded as of minor importance in lobar pneumonia as compared with serum or chemotherapy. In suffocating pneumonia, such as in capillary bronchitis; in wet hæmorrhagic pneumonia, as in influenza; in pneumonia after corrosive gases; in asthma complicated by pneumonia, or in pneumonia complicated by acute bronchiolar spasm—in these forms oxygen may be the most important item in treatment.

Properly administered, oxygen inhalation is compatible with any other form of treatment. It should never substitute for specifics when such are at hand.

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The idea of the 'combined' book is such an obvious one that it is surprising that the practice of combining the subjects has not been followed oftener; we can see only one real objection—the extra strain on the students' wrists, and many advantages, for ninety per cent of the pathological conditions that are peculiar to women have some direct association, before, during, or after the event, with child bearing. The division between pathological obstetrics and gynaecology is really a very artificial one.

The book is as complete a treatise on the subject as the student or the practitioner can wish for, and is designed to supplement the clinical lectures and practical demonstrations which the student will attend. Over a hundred pages are devoted to the anatomy and physiology of the reproductive organs. The division of the obstetric portion of the book is the usual one, into normal pregnancy, pathological pregnancy, normal and abnormal labour, the puerperium and the infant. There are short chapters on obstetric operations and puerperal mortality. There is a section headed gynaecology. It seems to the reviewer that it would have been more in the spirit of the book to have avoided this heading and grouped the chapters in this section under some other major headings.

The section on gynaecological operations is short, as the book is not written for the benefit of the gynaecological surgeon. The last section is on radiology, and includes both diagnosis and treatment.

It is a pleasant book to handle and to read. The print is good and the illustrations numerous, clear and relevant. The subject is dealt with comprehensively and the authority of the writers is beyond dispute. It is a book well suited to practice in this country.

**FRACTURES AND OTHER BONE AND JOINT INJURIES.**—By R. Watson-Jones, B.Sc., M.Ch. (Orth.), F.R.C.S. 1940. E. and S. Livingstone, Edinburgh. Pp. xii plus 723, with 1,040 photographs, x-rays, and diagrams, many of which are in colour. Price, 50s. Postage, 1s.

CONSIDERING the great importance of the subject, it is surprising to note that this new book is the first really thorough treatise on fractures and allied conditions to be written by a British surgeon. That it is the work of Watson-Jones of Liverpool should be sufficient guarantee of its worth. He and his associates have in the past published many original articles of the highest value on pathology, treatment, and diagnosis. These, together with some new work, have been incorporated in this book. But the bulk of the book is taken up with principles of treatment and details of technique which, though undeniably 'as done at Liverpool', are also representative of what is being taught and practised in the best fracture clinics throughout Great Britain.

The first part of the book describes the principles of fracture treatment, and includes the discussion of a complication of fractures to which the term avascular necrosis is given. Through loss of its blood supply, bone and articular cartilage undergoes immediate necrosis and may subsequently pass through the stages of regeneration and healing. The condition is recognisable radiologically only during the second and third months, when the necrotic bone which still retains its calcium, appears dense by contrast with the decalcifying living bone. The fractures, dislocations, and fracture-dislocations that are peculiarly liable to this complication are described in detail. In certain instances timely excision of bone which has undergone avascular necrosis is advocated. For instance, although an avascular fragment of a fractured scaphoid will unite if the wrist is immobilized for sufficiently long, the author is now of the opinion that better function and less arthritis result from excision of the fragment directly there is evidence that avascular necrosis is taking place.

Also worthy of special remark is a short section on the reduction and immobilization of fractures, which includes a careful description of plaster technique. For

walking plasters of the lower limb a metal stirrup is not favoured, because most patients acquire a bad gait. A leather boot of standard appearance, but made to fit over the plaster, gives better results.

Part II deals with pathological and birth fractures, and parts III to V describe fractures, sprains, and dislocations of each region in turn, the profusely illustrated text showing not only the correct treatment but also 'how not to do it'.

In part III, concerned with injuries of the trunk and head, the author's technique for reduction and immobilization of spinal fractures, already well known, is given in detail; also a new method of treating spondylolisthesis by manipulation is described. In addition, concise information is presented on two conditions which hitherto have received more attention in America than in Europe—painful affections of the lower back, and retropulsion of the intervertebral discs.

Mention must also be made of the author's operation for recurrent dislocation of the ankle. Briefly stated, this consists of the use of the peroneus brevis tendon for tenodesis and ligament reconstruction at the outer side of the ankle. From its very nature the operation must be open to the same objections as those of Hey Groves or Alexander Edwards' operations on the knee, and these are given but brief and unfavourable comment in this book.

Part VI is a collection of unusual and instructive cases, and the book ends with an appendix describing the organization of a fracture service, with photographs and plans from the Liverpool Royal Infirmary. Perhaps it would be possible, in a future edition, to reproduce an illustration of one of the case records from this fracture clinic, for they are marvels of clarity and completeness.

The book is a delight to handle. The publication has been beautifully done; the illustrations are excellent, the text almost entirely free from errors, and there is a generous bibliography. It should be in the hands of everyone who has much to do with fracture cases.

W. McN. N.

**DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY.**—By H. Bailey, F.R.C.S. (Eng.). Seventh Edition. 1940. John Wright and Sons, Limited, Bristol. Pp. xii plus 310, with 377 illustrations, some of which are in colour. Price, 21s.

THE last edition of this book was published in 1937 and was reviewed very favourably in our January issue of 1938. There is little more for us to add to what has already been said regarding the earlier edition, except that further improvement has been effected. There is one quite pleasant innovation; whenever the name of any syndrome, test, sign, structure, or instrument that has any proper name attached to it, Plummer-Vinson syndrome, Murphy's kidney punch, Douglas's pouch, etc., is mentioned a short, one-line, biographical note is added to help the reader to visualize the individual referred to, but he is given the option, and if he doesn't want to have his train of thought disturbed by place-names and dates he needn't, for the information is conveyed in a footnote. Douglas for example was a physician to Queen Caroline and died in the year 1742; his name conjures up the picture of a fashionable bewigged physician, but not so that of Dr. Murphy of Chicago.

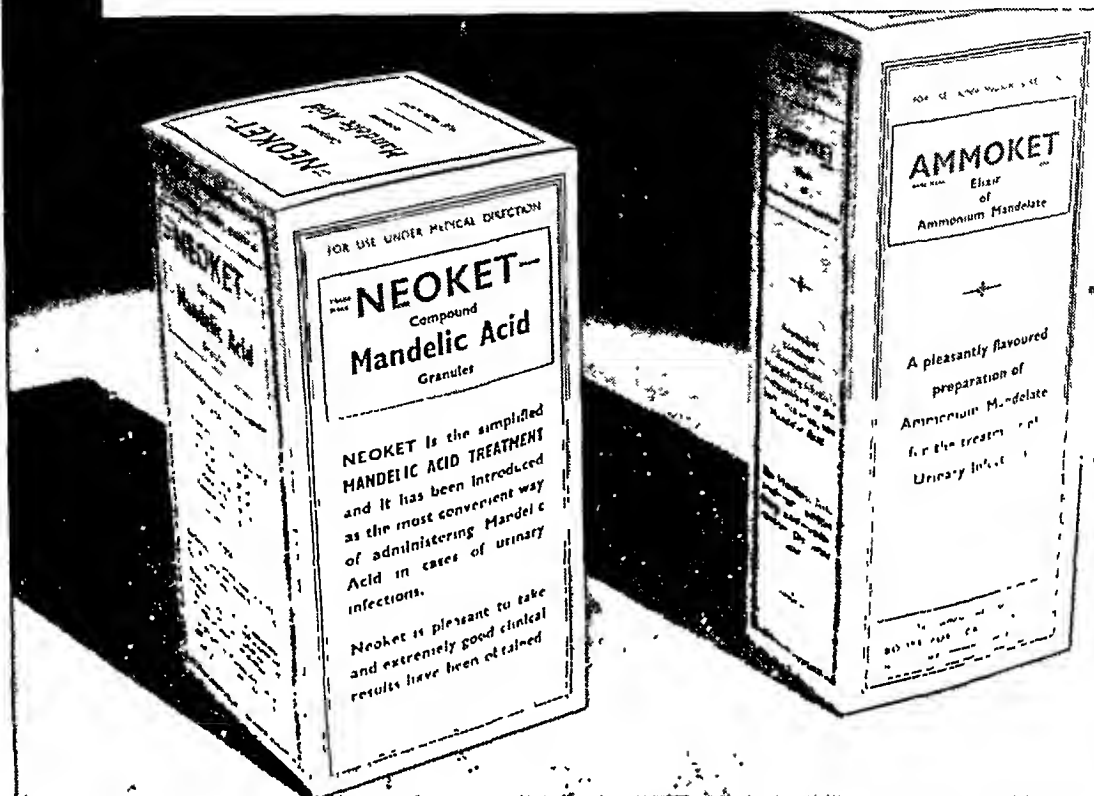
The scope of the book is completely expressed in its title, for every sign is not only described but demonstrated by beautiful photographs; many of these are in colour and are excellently reproduced.

The new generation of students have much to complain about in the length of the curriculum, but they are lucky to have books of this kind to help them over the early stages of clinical work.

We strongly recommend this book to the medical student and to his teacher. For the practitioner it is an ideal book of reference.



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The book is a masterpiece of compression; the art of the writer lies in the fact that truth is so seldom sacrificed to the exigencies of space, but occasionally this is inevitable. For example, it is stated that blood transfusion is 'the ideal method of treating anæmia'; the word 'surgical' would have saved the truth of this statement. The next few lines will also make the physiologist rub his eyes, when the words appear to read 'the blood contains hæmolysin and agglutinins which may cause dangerous clotting if . . .', but it is there, though the italics are ours.

This new edition of this invaluable book will be welcomed by final-year medical and post-graduate students.

**SCLEROSING THERAPY: THE INJECTION TREATMENT OF HERNIA, HYDROCELE, VARICOSE VEINS AND HÆMORRHOIDS.**—Edited by Frank C. Yeomans, M.D., F.A.C.S., M.R.S.M. (Lond., Hon.). 1939. Ballière, Tindall and Cox, London. Pp. xii plus 337, with 185 illustrations and 117 figures. Price, 27s.

It will be generally agreed that sclerosing therapy has emerged from the stage of experiment and empiricism. A practical monograph will, therefore, be acceptable to a large body of medical practitioners.

This book consists of four parts. The injection treatment of hernia is discussed by Dr. A. F. Bratnd in part 1 comprising eleven chapters. The chapter on the result of this method of treatment will be found very interesting. There is only one chapter in part 2 and this is on hydrocele and is written by Dr. G. F. Hoch. There is however no mention of hydrocele of filarial origin. Part 3, by H. J. Sheely, consisting of 15 chapters is devoted to the treatment of varicose veins. The author has recommended several solutions so that one may 'become well enough acquainted with these to be able to select the solution suitable for the individual case as well as for the different veins in the subject'. In the last part, the injection treatment of hæmorrhoids is fully discussed by the editor.

This is an instructive little volume which will be found useful by the general medical practitioner. The printing, get-up and illustrations are very good. The bibliography at the end of each part and the index will be appreciated by the inquirer. The price of twenty-seven shillings will not meet with general approval in these hard times.

P. N. R.

**MATERIA MEDICA, PHARMACY, PHARMACOLOGY AND THERAPEUTICS.**—By William Hale-White, K.B.E., M.D. (Lond.), M.D. (Dub.), LL.D. (Edin.). Revised by A. H. Douthwaite, M.D., F.R.C.P. Twenty-fourth Edition. 1939. J. and A. Churchill, Limited, London. Pp. xi plus 550. Price, 12s. 6d.

THERE has been a steady demand for this book for nearly half a century and it has reached its twenty-fourth edition in 48 years; the biennial regularity of the appearance of successive editions has seldom been disturbed.

The most satisfactory part of this book is the thorough pruning to which it has been subjected from time to time, so that, although much new matter has been included and entirely new subjects, such as vitamins, have been added, the book has not grown in bulk; if the reviewer's impression is correct, the present volume is actually smaller than the edition he used 25 years ago as a student. One of the main savings has been in the descriptions of the physical properties of crude drugs, and, once more to introduce a personal note, the reviewer never remembers at any time exercising the knowledge on this particular aspect of the subject that he gained so laboriously—though it had its lighter side; it is satisfactory to know that the student of the present day, who has a far fuller curriculum than we had, is at least spared this.

The most important additions are, naturally, the sulphanilamides; others are tetrachlorethylene (perhaps a little belated), nicotinic acid, and the sex hormones. The book has been revised throughout wherever this

was necessary and the information, as far as the reviewer was able to judge, is accurate and up to date. It is still the most useful and practical book of its kind for both the physician and the student.

**HANDBOOK OF PHYSIOLOGY AND BIOCHEMISTRY.**—By the late W. D. Halliburton, M.D., LL.D., F.R.C.P., F.R.S., and R. J. S. McDowall, M.D., D.Sc., F.R.C.P. (Edin.). Thirty-sixth Edition. 1939. John Murray, London (Albemarle Street). Pp. x plus 977. Illustrated. Price, 18s.

THIS book has served four generations of students and is now a nonagenarian but, we hurriedly add, a nonagenarian completely rejuvenated. In recent years, editions have appeared regularly at two-year intervals. There have been no striking changes in the present edition but all recent advances in our knowledge on the subject have been skilfully interwoven in the text of the previous edition.

The book is too well known to require any detailed description. It is a book that has always exercised a special appeal to the student and his teacher; it is easy to handle and easy to read; it is well illustrated and the text is concise and clear; and finally the authority of the present author is unimpeachable.

**TEXTBOOK OF PATHOLOGY. A CORRELATION OF CLINICAL OBSERVATIONS AND PATHOLOGICAL FINDINGS.**—By Charles W. Duval, M.D., and Herbert J. Schattenberg, M.D. 1939. D. Appleton-Century Company, London. Pp. xxii plus 681, with 12 plates and 377 illustrations in the text. Price, 35s.

WITH the publication of this new textbook on pathology another addition is made to the long list of books on the subject from which the student has to make his choice. There is much to commend this book both to the student and the teacher. The authors have stressed the relationship between pathological physiology and altered tissue changes or morbid anatomy. There is in this book the proper blending of the morgue pathology with clinical medicine, with the result that subject is dealt with in a more comprehensive manner than in the restricted and narrow concept of pathology, in the full justification of the sub-title—a correlation of clinical observations and pathological findings.

All the usual subjects are included and dealt with under different systems. At the end of the book there is a useful chapter on autopsy in which the methods employed in the post-mortem room are detailed with a protocol giving an example of an autopsy report. The illustrations must be specially mentioned. There are excellent half-tone and coloured plates and many photographic illustrations. These are of exceptional excellence; they show the changes intended to be shown and prove that photography of pathological lesions is capable of giving satisfactory results. The publishers are to be congratulated on their most satisfactory reproduction.

This is a book that is certain to take a place among the best books on the subject and can be confidently recommended to the medical student.

C. L. P.

**HUMAN HISTOLOGY: A GUIDE FOR MEDICAL STUDENTS.**—By E. R. A. Cooper, M.D., M.Sc. 1939. H. K. Lewis and Company, Limited, London. Pp. xlv plus 423, with 237 illustrations. Price, 16s.

THE idea of this book is a good one; it is to provide the medical student with a handy guide to the elements of histology that will be suitable for use in his practical histology classes, just as he uses his 'small Cunningham' in the dissecting room. The book should serve this purpose very well, but there is a little more in it than this, for the student will find it useful in later years, when he studies pathology.

The explanations are concise and clear, and the book is profusely illustrated with photographs of sections. These show what they are supposed to show and do not leave too much to the imagination; on the other

A specialist in Tropical Medicine, addressing a meeting of eminent malariologists, recently stated:

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hand they are the real thing and therefore much better than line drawings, which merely show the student what he ought to see, but seldom does. For the sake of the student, it is necessary to be precise, sometimes to the sacrifice of recent work which the writer may feel has not quite reached the stage of digestion suitable for students; this is probably what he felt about recent work on the spleen. Surely, the main blood storage is in the sinuses themselves, and in an emergency we depend on these and not on the few red cells that have wandered into the reticular spaces in the pulp.

This is a book that should be particularly useful for class work in this country, for it will supply the student for the Indian university degree with as much as he will require on the subject for his examination; he will also find it a useful book of reference.

**AN INTRODUCTION TO PATHOLOGY AND BACTERIOLOGY FOR MEDICAL STUDENTS IN THE TROPICS.**—By E. C. Smith, B.A., M.D., D.P.H., Sc.D. (Dublin), M.R.C.P. (Lond.), M.R.C.P.I., D.T.M. & H. (Eng.). 1939. John Bale Medical Publications Ltd., London. Pp. xiv plus 279, with 18 plates and 77 illustrations in the text. Price, 15s.

THE author wisely states in the preface that the book is not to be regarded as a substitute for the many excellent textbooks available but rather as an introduction to them. It is therefore difficult to understand why space which could have been more profitably utilized is taken up for depicting certain well-known laboratory apparatus. In reading through the text one comes to the general conclusion that there are many sections, too numerous to enumerate in a review, which have received but scanty treatment and which a student would find difficult to understand. Cholera, a disease of such major importance in the tropics, is disposed of in one page, botulism, a disease fortunately rare in the world and rarer still in the tropics, receives the same amount of space. The section on diseases caused by helminths particularly needs to be revised. There are many vague statements which would confuse the student. With judicious pruning and enlarging a book of this type would be of great value to the student of medicine in the tropics. There is a real need for a small book on pathology which stresses points of particular interest and importance in the

tropics, but in its present form this book cannot be recommended to the medical student.

C. L. P.

**INDIAN MEDICAL SERVICE: A HANDBOOK.**—By Major A. N. Chopra, I.M.S. 1939. Government of India Press, New Delhi. Pp. vi plus 256. Price, Rs. 2 or 3s. (Obtainable also from Provincial Government book depots and stockists of Government publications)

THIS little handbook contains a vast amount of useful information ordinarily scattered in different Government publications, or contained in various circulars which often are not available or in which the required information is difficult to find. Major Chopra has done a great service to his brother officers of the Indian Medical Service in bringing together, arranging, and indexing the various rules and regulations which govern the Service, together with a great deal of useful information of interest and value to all Government servants.

From the foreword by Major-General Bradfield it is noted that a handbook on the Indian Medical Service was published in 1890 and the next publication of this type was in 1912. The present handbook is published more than a quarter of a century later. It is incomprehensible to the reviewer that if the predecessors of this handbook were anything on the lines of the present publication that there was not a demand for more frequent issues of this type of book. It is to be hoped that revised editions will be issued periodically.

The book is divided into eleven well-arranged chapters dealing with recruitment into the Service, promotion, courses of instruction, leave, pay and allowances, passages, funds and ending with pensions. There are in addition seventeen appendices which contain a mass of useful information. This handbook will be of great value to all members of the Service. It should also find a place in the libraries of all medical schools where it will be of interest to all who aspire to enter the Service. There is only one thing that the reviewer would wish to add in a book of this type and that is a small chapter giving a brief outline of the history and the outstanding achievements of the Indian Medical Service.

C. L. P.

## Abstracts from Reports

### REPORT OF THE DIRECTOR OF MEDICAL SERVICES, HONG KONG, FOR THE YEAR 1938

THE year 1938 was marked by the prevalence and persistence of infectious diseases in the colony. At the end of 1937 smallpox had begun to attain epidemic proportions and the number of cases notified increased rapidly in the early part of the year, reaching a maximum in March. The last case of this series was notified in July and by the end of that month the disease had died out.

Cholera recurred in Hong Kong in 1938, the first case being notified on the 25th May. The disease was not as widespread as in 1937, thanks in part to the rigorous measures of control which were adopted, and in part to the fact that the disease was expected and everything was in readiness to combat an outbreak.

A sudden sharp rise in the number of cases of epidemic cerebro-spinal meningitis was also noted shortly after the inflow of starving refugees and this was probably due to the fact that these people were brought into contact with carriers of the disease in the colony and, being exhausted and ill-fed, succumbed to it readily.

Malaria, thanks to the malaria bureau, is no longer to be regarded as one of the major killing diseases in Hong Kong. Control is still essential as the infection rate remains high in rural areas which cannot be freed from breeding places, for economic reasons. The number of deaths recorded from malaria in 1938 is 733; this number includes two deaths from malaria among the forces of the Crown. No case of blackwater fever was recorded. Nine cases of filariasis and five of dengue were reported during the year. It is clear, therefore, that the incidence of mosquito-borne disease in Hong Kong is not excessively high.

No case of plague was recorded in Hong Kong in 1938: the infection appears to have been absent from the colony since 1929.

Typhus occurred in epidemic form in several parts of northern China during the spring months, but Hong Kong was fortunate in having only two cases during the year. One was a naval rating who appeared to have contracted his infection in Shanghai, twelve days before arriving in Hong Kong; the other was a young male refugee who developed the disease three days after arriving from Shanghai.

Approximately one out of eight of all deaths occurring in Hong Kong in 1938 was due to pulmonary tuberculosis, which killed 4,920 people in the year. It is probable that at least five people suffer from the disease for every one who dies of it, and the opportunities afforded for its spread by overcrowding are legion.

Dysentery was rife throughout the year and accounted for 338 deaths out of a total of 1,071 cases. There was no significant rise in the number of cases before the cholera epidemic began.

Numerous cases of typhoid fever were reported during the autumn months. The disease was in the majority of cases due to *Bacterium typhosum*, and killed 187 people out of a total of 539 cases. The months of maximum incidence were June and July, with 79 and 92 cases respectively.

#### ANNUAL PUBLIC HEALTH REPORT OF THE PROVINCE OF BIHAR FOR THE YEAR 1937. BY LIEUT.-COLONEL S. L. MITRA, D.P.H., I.M.S., DIRECTOR OF PUBLIC HEALTH

*Comparative incidence of the chief diseases.*—The undermentioned statement compares the ratios under the chief heads of mortality in 1937 with the average ratio of the previous ten years:—

	URBAN		RURAL		COMBINED	
	Ten years' average	1937	Ten years' average	1937	Ten years' average	1937
1	2	3	4	5	6	7
Cholera .. .. .	0.8	0.3	1.5	0.4	1.5	0.4
Smallpox .. .. .	0.5	0.3	0.5	0.2	0.5	0.2
Plague .. .. .	0.05	0.04	0.1	0.05	0.1	0.04
Fevers .. .. .	6.8	6.6	17.3	18.5	16.9	18.1
Dysentery and diarrhoea .. .. .	0.5	0.8	0.1	0.09	0.1	0.1
Respiratory diseases .. .. .	0.5	0.7	0.1	0.08	0.1	0.1
Injuries .. .. .	0.5	0.5	0.3	0.3	0.3	0.3
All other causes .. .. .	4.3	4.8	3.3	3.2	3.4	3.2
TOTAL ..	14.1	14.0	23.4	22.9	23.0	22.5

The death rate has increased from 21.7 in 1936 to 22.5 per mille of population in 1937. The increase in the number of deaths was due chiefly to comparatively larger number of deaths from cholera and fevers, the death rates from these being 0.4 and 18.1 as against 0.2 and 16.9 of the previous year. The highest death rate 18.1 was recorded from fevers. Deaths from malaria are included under the heading of 'Fevers' and as malaria prevailed in epidemic form in several districts of the province during the year under review, it is presumed that the increased death rate from fevers was chiefly due to greater number of deaths from this disease.

#### A REPORT OF THE SIXTY-FIFTH YEAR'S WORK IN INDIA AND BURMA OF THE MISSION TO LEPERS

*September 1938 to August 1939*

A COMPARISON of figures shows that the expenditure in India and Burma upon the Mission's work was Rs. 8,42,535 in 1938, as compared with Rs. 8,12,209 in

1937. Of this total Rs. 4,10,688 was contributed by voluntary gifts, of which well over three and a half lacs of rupees came from supporters in other countries. Since the superintendence of the homes is, in almost every case, a voluntary service rendered without charge to the Mission to Lepers, this means that practically the whole of the income is set free for the care of the lepers, and the maintenance of the local staffs. This almost complete absence of overhead charges for superintendence is the reason why, with a little over eight lacs of rupees, the Mission was able to maintain 7,565 lepers resident in its thirty-four homes, and 834 healthy children of lepers brought up separately. It was also able to make grants-in-aid of substantial character to other homes with 2,270 leper inmates and 151 healthy children. The gross total of 10,820 compares with 10,590 on the same date in 1937, showing a continued increase of the numbers helped.

Much of the growth in the Mission's work during the last year has been in the care of greater numbers of children suffering from leprosy. At the end of 1937 there were 560 such children in our care; at the end of 1938, 678. This increase in numbers has, of course, to be matched by the provision of increased accommodation. Just after Christmas last the new Dublin Ward for girls with leprosy in its contagious form was opened at Purulia, Bihar. This is a welcome addition to the special accommodation for children in this home.

Last October saw the opening by the Minister of Health for Madras of a new home for healthy children at Vadathorasalur, releasing the old home for the use of children with leprosy, so that altogether some 130 children are being cared for at this station. At Cuttack the King George V Memorial wing for boys with leprosy, and given by the people of the Province, was opened in March this year by His Excellency the Governor of Orissa, and is already serving a most useful purpose. And at Rawalpindi the erection of a home for healthy children was just being completed as the period covered by this report closes.

Another encouraging feature of the year's work has been the success which has attended the first twelve months of the life of the new leper home at Zamurradganj, near Fyzabad, opened in August 1938. There is a considerable waiting list for admission, and there is a large out-patient department.

The main building work engaged in during the year, apart from the additions recorded in the paragraph touching on children's work, has been in the building of the first part of a new hospital section at the Naini Leper Home, Allahabad. The women's wing is complete and the medical administration block is



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\**B.M.J.*, 1937 August 28. Page 412.

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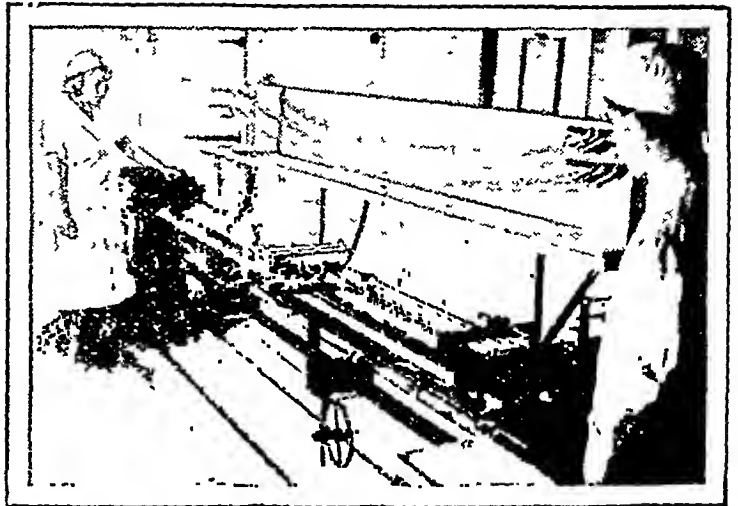
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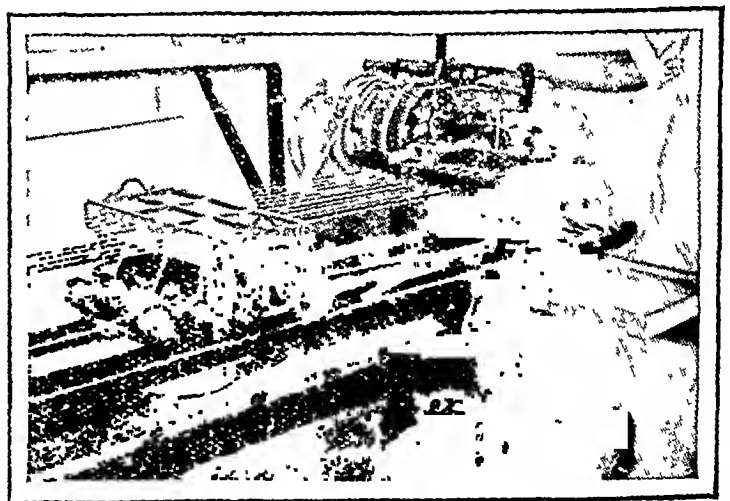
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quickly going up. Funds were also granted to enable an out-patient clinic to be provided at Sholinghur, and for another at Arkonam, both in the Madras Presidency. A grant was made towards the rebuilding of the aided home at Narsapur also in Madras, where the cyclone of November 1938 did great damage. The Assembly Hall at Kothara, Ellichpur, in Berar, has been enlarged, and an administration building provided. And at numerous homes small projects have been undertaken, such as extension of staff quarters or improvement of water supply, which, though not large individually, make up in the total a considerable addition to the equipment of the homes.

The medical work of the Mission continues to give reason for a measure of encouragement. That 514 patients were discharged during 1938 with the disease arrested before deformity had begun (and a further period of six months passes during which the patient remains under observation after the last traces of activity have disappeared) is itself encouraging. At the same time the number of known relapses in 1938 from discharges in previous years—79—shows that 'arrest' is the proper term to use rather than 'cure'—a word which the Mission to Lepers has studiously avoided using during the years when optimism ran high, and claims were sometimes unguarded. The chief medical service which the Mission brings to the adult patient is, perhaps, by the fellowship and activities and regular conditions of living provided, which help to re-establish him into a life of happiness and usefulness, even within the bonds of his disease. For the children with only early marks of leprosy the Mission has evidence that it can do much more, enabling them to grow up into men and women who, with reasonable safeguards, should remain in good health. Its service to the community—and one which needs to be

emphasized because it is often forgotten—is in saving the public from the risk of infection from the thousands of contagious cases to whom the Mission extends its hospitality.

#### ANNUAL REPORT ON THE MEDICAL INSPECTION OF SCHOOL CHILDREN IN SIX TOWNS OF THE NORTH-WEST FRONTIER PROVINCE DURING THE YEAR JULY 1937 TO JUNE 1938

THE scheme of medical inspection of school children was extended to the Mardan Municipal Town and the work was actually commenced from the 1st September, 1937, when the schools had re-opened after the summer vacation. The scheme was also extended during the year under report to seven rural schools in the Province.

The total number of boys medically examined during the year under report was 21,267 and the annual recurring expenditure amounted to Rs. 9,278-8. Accordingly the expenditure per boy comes to Re. 0-7-0 per annum as compared with Re. 0-7-2 per annum during the previous year. The decrease in the expenditure of two pies per boy per annum does not call for any comment.

Out of a total of 16,808 cases recommended for treatment in the schools of the six municipal towns during the year 13,347 or 79 per cent actually received treatment.

In the girls schools in Peshawar City 552 cases were recommended for treatment and 388 or 70 per cent actually received treatment, while in the seven rural schools 887 were recommended for treatment and 737 or 83 per cent actually received treatment.

## Service Notes

### APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL R. V. MARTIN, C.I.E., to be Officiating A. D. M. S., Waziristan District. Dated 11th December, 1939.

Lieutenant-Colonel A. C. L. O's Bilderbeck to be O. C., C. I. M. H., Bannu. Dated 21st November, 1939.

Lieutenant-Colonel R. A. Warters to be O. C., I. M. H., Bangalore. Dated 11th December, 1939.

Lieutenant-Colonel H. M. Strickland to be Specialist in Radiology, Lahore District. Dated 28th December, 1939.

Lieutenant-Colonel S. M. Hepworth to be Specialist in Radiology, Madras District. Dated 30th November, 1939.

Lieutenant-Colonel G. R. Oberai, Superintendent, Central and District Jail, Benares, transferred to Central Jail, Naini, Allahabad, *vice* Major R. N. Bhandari (on leave).

Lieutenant-Colonel H. E. Murray, on return from leave, is appointed as Civil Surgeon, Hooghly, *vice* Captain E. H. Lossing.

Lieutenant-Colonel S. Nag (on leave) is appointed to be Civil Surgeon, Murshidabad, *vice* Dr. Sita Nath Ghosh, transferred.

Major C. A. Bozman is appointed as Port Health Officer, Bombay, with effect from the 4th October, 1939.

Major G. Y. Thomson to be Specialist in Ophthalmology, Deccan District. Dated 28th November, 1939.

Major S. S. Bhatnagar, an officer of the Medical Research Department, is appointed as a leave reserve officer under the Central Government, with effect from the 24th December, 1939 (forenoon), and is attached to the Haffkine Institute, Bombay, as a Supernumerary Officer.

Major R. McRobert, Civil Surgeon, Monywa, on transfer, relinquished charge of his appointment on the forenoon of the 27th January, 1940.

On completion of the period of his probation, Captain S. P. Bhatia is confirmed in his existing appointment as Deputy Assistant Director-General (Medical Stores), Calcutta, with effect from the 20th June, 1939.

Captain C. L. Greening is transferred to the Civil Branch of the Indian Medical Service, and is appointed to the Medical Research Department on probation for 2 years, with effect from the 20th December, 1939 (forenoon), and is posted to the Central Research Institute, Kasauli, as a leave reserve officer under the Central Government.

Captain L. S. F. Woodhead is transferred to the Civil Branch of the Indian Medical Service, and is appointed to the Medical Research Department, on probation for 2 years, with effect from the 21st December, 1939 (forenoon), and is attached to the Pasteur Institute, Shillong.

Captain R. L. Haviland Minchin, a leave reserve officer against the Central Indian Medical Service Cadre, is appointed Assistant Director, Central Research Institute, Kasauli, with effect from the 23rd December, 1939 (forenoon), *vice* Major S. S. Bhatnagar, transferred.

Captain V. M. Albuquerque to be Specialist in Surgery, Presidency and Assam District. Dated 26th December, 1939.

Captain E. H. Lossing, on relief, is appointed as Civil Surgeon, Rajshahi, *vice* Dr. Satya Charan Sen.

### LEAVE

Lieutenant-Colonel S. L. Bhatia, M.C., Principal, Grant Medical College, and Superintendent, J. J. Group

of Hospitals, Bombay, has been granted leave on average pay for 2 months in India, with effect from the forenoon of 15th January, 1940.

Major J. H. Boulbee on further extension of sick leave up to 30th April, 1940.

#### PROMOTIONS

The undermentioned Indian Medical Service Officer is advanced to the List of Special Selected Lieutenant-Colonels:—

Lieutenant-Colonel E. W. O'G. Kirwan, C.I.E. Dated 17th October, 1939.

*Brevet-Lieutenant-Colonel to be Lieutenant-Colonel*

A. H. Craig. Dated 23rd December, 1939.

#### *Captains to be Majors*

S. W. H. Askari. Dated 3rd January, 1940.

Hoe Min Sein. Dated 26th January, 1940.

A. E. Kingston. Dated 1st February, 1940.

G. K. Graham. Dated 3rd February, 1940.

A. W. West. Dated 3rd February, 1940.

#### *(Short Service Commission)*

#### *Lieutenants to be Captains*

I. Singh. Dated 12th January, 1940.

D. Bhatia. Dated 12th January, 1940.

N. D. P. Karani. Dated 12th January, 1940.

Nowshir Jungalwalla. Dated 1st February, 1940.

Dharam Dev Varma. Dated 1st February, 1940.

H. Rees. Dated 27th September, 1939, with seniority from 1st May, 1938.

#### *Lieutenants (on probation) to be Captains (on probation)*

Dated 27th September, 1939, with seniority from 1st November, 1938

S. G. Nardell. D. H. Harrison.  
K. D. Fraser.

Dated 27th September, 1939, with seniority from 1st May, 1939

G. S. Michelson. P. J. Wormald.  
J. Aitken. G. T. M. Hayes.  
P. Kent. J. P. O'Riordon.  
R. O. Yerbury.

Dated 19th October, 1939, with seniority from 1st September, 1939

A. S. Brown.

#### RETIREMENTS

Colonel W. E. R. Williams, O.B.E., K.H.S. Dated 29th January, 1940.

Colonel R. S. Townsend, M.C. Dated 10th November, 1939.

## Note

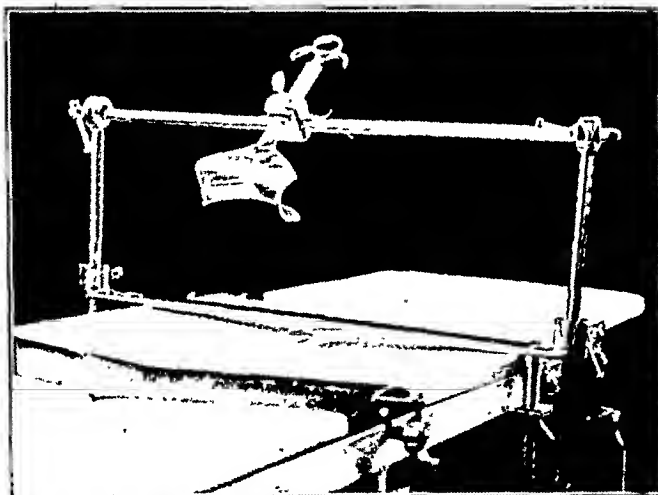
### RETRACTOR STAND

THE 'retractor stand' shown here was specially made for me by Powells Limited, Surgical Instrument Makers, Bombay; I have devised this stand for deep pelvic and other abdominal operations.

In deep pelvic and other abdominal operations, in which both a firm hold and a large field of vision are required, this stand obviates the need for the services of a third assistant, holding a retractor.

There is already on the market a stand which is placed between the legs of the patient, but in actual practice it is unsatisfactory in several ways. For instance, it greatly interferes with the proper arrangements of sterilized towels, and causes unnecessary pressure in the patient's groin. It also prevents the

passing of a catheter or rectal or vaginal instrument, so often required during the course of an operation.



The new stand does away with all these difficulties, and greatly facilitates surgical manoeuvres.

J. R. PARAKH, M.D., M.R.C.S.

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## Original Articles

### COMPARISON OF THYMOL AND SOME OTHER DRUGS IN THE TREATMENT OF HOOKWORM INFECTION

By P. A. MAPLESTONE, D.S.O., D.Sc., M.B., B.S., D.T.M.  
and

A. K. MUKERJI, M.B.

(From the Helminthological Research Laboratory,  
School of Tropical Medicine, Calcutta)

Up to a little more than twenty-five years ago thymol was the only efficient drug at our disposal for the removal of hookworms. Since then there have been successively introduced beta-naphthol, oil of chenopodium, carbon tetrachloride, tetrachlorethylene and hexylresorcinol, all of which have had their advocates, but in common with thymol none of them are free from certain disadvantages, and it is in the assessment of the disadvantages against the efficiency of these various drugs that considerable disagreement has arisen.

Lane (1935), who, from his published work, seems to have had personal experience with thymol only, reviewed most of the important work on these anthelmintics published up to that date and his main conclusion is as follows: 'It seems to leave thymol in the first place, especially when safety and efficiency are both considered, it being again stated emphatically that *safety must have the first place*'. He also says:—'The bulk of what has been offered as evidence for appraising hookworm-killing drugs has been reached in non-comparable ways', and he ends his paper by expressing the hope that its publication will lead to the collection of further evidence based on strictly comparable results. The same author (1936) covered the same ground in slightly more popular language, but neither of these papers appears to have induced anyone in a position to do so to carry out such a series of comparative observations. Possibly most workers with experience of the post-thymol drugs did not think it worth while following Lane's suggestion. Although not in agreement with much of what Lane said, we felt that at least his criticism of the absence of strictly comparable results in assessing the value of these anthelmintics was justified. Accordingly very soon after the publication of his first paper we commenced a comparative investigation of some of the drugs reviewed by him and have only recently completed the work.

The reason this work took so long to complete was that we wished to make our results as definite as possible, and to ensure this several factors had to be taken into account.

It was considered advisable to include only those persons who had an appreciable hookworm infection because very light infections are usually much more easily eradicated than heavy

ones. We decided upon an egg count of 1,000 eggs per c.cm. of stool as the standard of infection that must be reached and in only two cases were lighter infections included. The number of heavily-infected persons in Calcutta is small, so it took us a long time to collect sufficient for our purpose.

Another necessity was that the patients had to be willing to come into hospital and to remain for an indefinite period, which still further extended the time of these observations.

There were three reasons why we only considered in-patients:—

(a) There was no chance of reinfection during the period of observation.

(b) The stools could all be saved after treatment and thus the species of all the worms passed could be determined. This is important because all the evidence available points to the fact that ancylostomes are more difficult to eradicate than necators, and as we have both species in Calcutta it was felt that our results might be weighted, either favourably or unfavourably, in respect of any of the drugs used, if the species of all the worms removed were not known.

(c) Daily examination of the stools by D.C.F. was possible, and this was carried out from the day after treatment in every case for as long as was required, and this method of examination was supplemented by egg counts, when the latter were indicated according to our plan of investigation.

On account of the difficulties in obtaining enough patients in a reasonable time we have confined our investigation to three of the drugs discussed by Lane. Even limited in this way the work has taken over three years, and if all the drugs had been included this period would have been extended to several years more. This was considered unjustifiable in view of the probably slight value of the extra information that would have been acquired, and so we have confined our comparison of thymol with the two drugs, which from our personal experience, we consider most worth while. The drugs we have tested are thymol, tetrachlorethylene alone and tetrachlorethylene and oil of chenopodium given together.

Carbon tetrachloride has not been tested because it is undoubtedly more dangerous than tetrachlorethylene, and our own earlier investigations carried out with these two drugs on comparable lines showed that there was little to choose between them regarding efficiency (Maplestone and Mukerji, 1929, 1933, and 1937).

Oil of chenopodium alone has not yet been examined, but our figures given in this paper when it is used with tetrachlorethylene, compared with those achieved by tetrachlorethylene alone, suggest it is not as good as other workers have claimed. However, we do not feel prepared to dismiss it as Lane (1935) has done with the remark, 'I can find no acceptable published

evidence of its efficiency against hookworms', and we have already commenced a series of treatments with it, carried out on exactly the same lines as have been followed in this paper, the results of which will be published in a supplementary paper.

Hexylresorcinol was found by us (Maplestone and Mukerji, 1932) to be so inefficient in the few cases in which we tried it that, coupled with its relatively high cost and the need for preliminary restriction of diet in the patient, we do not consider it worthy of consideration against the other anti-hookworm drugs available.

Beta-naphthol has not been tried because we agree with Lane (1936) that it is inefficient in safe doses and toxic in doses sufficiently large to remove the majority of worms. In any case, this drug has never been widely used for this purpose.

#### *Methods of administration of the drugs*

*Thymol.*—Lane has pointed out that much of the disrepute into which this drug has fallen may be accounted for by the fact that it has been given in large crystalline lumps and not finely divided and mixed with a suitable excipient to prevent it again adhering into a single mass after division, because it has been shown that this measure greatly improves its efficiency. The two excipients recommended by different workers are sodium bicarbonate and lactose. We used both of these together, taking ten grains of sodium bicarbonate in all cases and adding to it enough lactose to make the mixture equal in weight to the dose of thymol being given in each case. This was done shortly before the administration of the drug, and the prepared mixture was placed in as many hard gelatin capsules as were needed to contain the dose. The dose was given in two parts with an interval of one hour and a half between them and followed one hour and a half later by a dose of two ounces of saturated sodium sulphate solution. The stools were always searched for the capsules to make sure they had opened in the intestinal tract. It should be noted that none of our cases received the full dose of 60 grains recommended for adults, because all of them were debilitated and under-weight, so the dose for each person was calculated to the nearest grain on a basis of 60 grains of thymol for 150 pounds of body-weight, which is a more accurate method of administering drugs, in which the dose must be limited for safety, than to base the dosage on years of age. This method of graduating the dose is recommended by Chopra and Chandler (1928) who based their recommendation on an age-and-dose-table compiled by Ashford and King, two authorities who probably had a wider experience of thymol than anyone else.

*Tetrachlorethylene.*—The whole dose was shaken up in two ounces of saturated solution of sodium sulphate and administered immediately, before it had time to coalesce again into larger masses as it rapidly does if left at rest.

Our idea in shaking the mixture in this way is that something the same effect as particulation of thymol is effected, and our opinion of the efficiency of tetrachlorethylene being thereby increased is based on our relatively poor results with this drug when we first used it and gave it in the soft gelatin capsules in which it was supplied, compared with our later results when we received it in bulk and could pour it direct into the sodium sulphate solution. Lane (1935) argues that our reasoning is unsound because he found that 4 c.cm. of tetrachlorethylene shaken up with two ounces of saturated sodium sulphate solution begins to separate out in ten seconds and nearly all had collected at the bottom of the flask in one minute. We have not been able to observe what goes on inside the stomach when a dose shaken up as we recommend it is swallowed, but we feel certain that the conditions in an actively motile and warm organ such as a normal stomach, which probably contains some food and mucus as well, is hardly comparable to the conditions in a glass flask standing motionless on a table at room temperature with nothing in it but the sodium sulphate solution and tetrachlorethylene. Such a criticism appears inconsistent with Lane's frequent insistence on strictly comparable conditions being a necessity before one can draw sound conclusions on the comparative value of two different observations.

The full dose of 4 c.cm. was given to all the persons in this series because our experiments on cats (Maplestone and Chopra, 1934) added to many years' practical experience in the use of this drug have led us to the conviction that this amount is so far below the dangerous limit that it can be given with perfect safety to adults who are well below the usually-accepted normal body-weight.

*Tetrachlorethylene and oil of chenopodium.*—These two drugs were shaken up in two ounces of sodium sulphate solution and given immediately in the same way as tetrachlorethylene alone. The dose given was 4 c.cm. of tetrachlorethylene and 1 c.cm. of oil of chenopodium. The oil was stated to be of British Pharmacopœia standard, which was confirmed for us by a skilled chemist.

#### *Methods of observation of cases*

Before undergoing treatment egg counts by Stoll's technique were made. We used a slight modification of Stoll's original method which we find gives better results. We take twice the amount of decinormal sodium hydroxide that Stoll does for diluting the stool, which is 1 c.cm. by cubic capacity instead of 1 gramme by weight, and the number of eggs found in two counts of the preparation are added together and multiplied by 100 to give the estimated egg content.

Cases were treated by the three drugs in rotation as they occurred, without any selection.

The complete stools passed for forty-eight hours after every treatment were saved and all



the worms passed collected and identified. This was done in all but two cases in one of which the stools were not saved and in the other no worms were found although it was apparently cured. These, as well as a few cases in which some of the worms were so broken as to be unidentifiable, are shown in the protocols.

From the day following treatment the stools were examined every day for ten days by D.C.F. if they did not show eggs sooner. If consistently negative for this time the case was classed as cured, but if it again became positive and showed an estimate of more than 100 eggs per c.cm. of stool it was again treated a fortnight after the previous treatment.

Unfortunately treatment could not be continued in every case until it was completely cured, because the demand for beds in our hospital is so great that they could not be accommodated for a sufficiently long period. Accordingly an arbitrary standard of reduction of infection was decided upon, below which no further treatment was given. As this was the same in all three series the uncured cases can be compared as well as the cured ones. Cases which showed not more than four eggs in a D.C.F. preparation were not treated again, and if there were more than four eggs by this method a dilution count was done. If no eggs were found in two preparations the case was classed as 'under 100 eggs' and if one egg was found in two preparations it was classed as '100 eggs' (per c.cm.). Neither of these classes were again treated, but every case that showed more than one egg in two counting preparations was again treated and the actual count was not recorded.

#### *Intensity of infection*

It will be seen in the table that the intensity distribution of infections, as indicated by egg counts and irrespective of species of worm, that the thymol group had nine cases with over 10,000 eggs per c.cm. compared with five in the tetrachlorethylene and 11 in the mixed treatment groups, that with between 9,000 and 1,000 eggs there were 14, 20 and 14 cases respectively, and that there were only two with less than 1,000 eggs, both in the thymol group. Although at first glance it might appear that the thymol group was the more difficult to cure compared with the tetrachlorethylene group on account of the higher number of heavy infections in it, comparison with the mixed treatment group especially, and the almost complete absence of any evidence of correlation between intensity of infection and number of treatments needed to effect a cure in all three groups, indicates that there is no significant difference regarding the probable difficulty in effecting a cure in the three groups.

#### *Species of worm*

In those cases which had more than two treatments the total number of which additional treatments (whether 3rd, 4th or 5th) was 44, only two necators were passed, one male in one

case and one female in another, both in the thymol group. After the same 44 treatments one or more ancylostomes were passed after 35, and after nine no worms of either species were seen. This accords with the generally-accepted view that ancylostomes are more difficult to get rid of than necators. With the limited number of figures available it is not possible to make any statistical estimate of the probable difference between the two worms in this respect. It is accordingly proposed to compare the three groups chiefly with regard to the intensity of infection and number of cases infected with ancylostomes only and to lay little stress on necators; the degree of infection in this portion of the paper is estimated by the actual number of worms found in the stools after treatment.

GRAPH 1

Species distribution of worms in individual cases in the three groups.



Note.—One case was cured but no worms were recovered in the mixed treatment group.

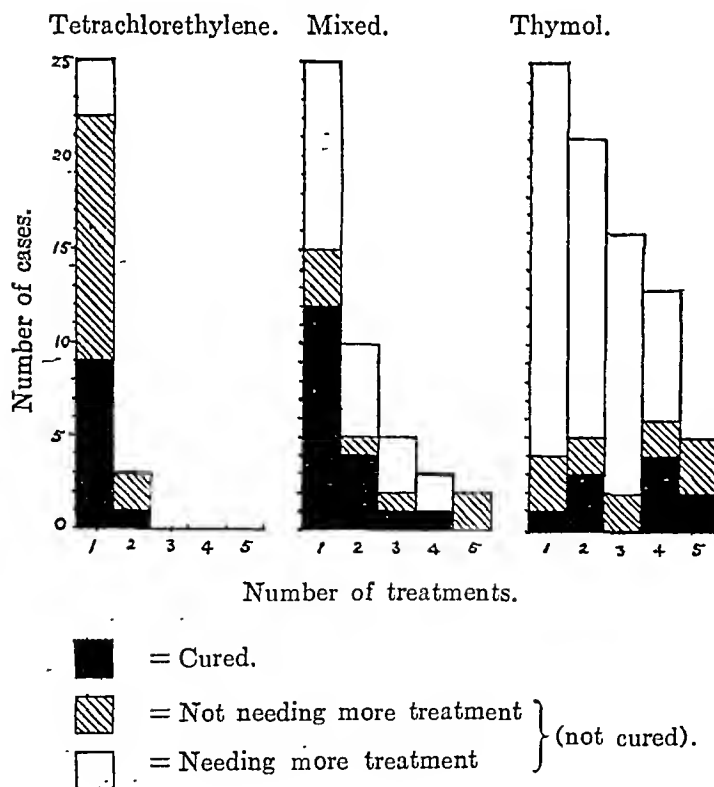
The stools were not saved in one case in the tetrachlorethylene group.

In the thymol group there were 17 infected with ancylostomes and 15 in each of the other groups: in one tetrachlorethylene group case the stools were not saved and in one mixed treatment no worms were found though the case was cured by one dose of anthelmintic.

It is evident from graph 1 that thymol had to deal with a larger number of fairly heavy ancylostome infections than either of the other groups although the three heaviest infections were in the latter. Even if it is admitted that on this account thymol appears in a less favourable light in comparison with the other forms of treatment, the differences are not sufficiently great to account wholly for the great difference

in the results. This is borne out by more detailed examination of the protocols. In the first place only one case was cured by one treatment in the thymol group and only three others were reduced sufficiently not to need further treatment, and in this group there were eight pure necator infections. Further, after three treatments, all except four of which were with thymol, five cases remained which required one or two additional treatments to effect a cure or to bring them to the no-further-treatment level. Examination of the tetrachlorethylene group shows that this drug cured nine in one treatment and that five of these had ancylostome infections, also an additional eight had ancylostomes out of 13 which were brought to the no-further-treatment level by one treatment. This left only three needing a second treatment and of these one was cured and the other two were brought to the no-further-treatment level; the mixed treatment group is in some respects superior to the tetrachlorethylene group, but five cases needed more than two treatments.

GRAPH 2  
Results of treatment.



The difference in results is just as clearly shown in another way in graph 2. Expressed in figures this reveals that in the tetrachlorethylene group a total of 28 treatments cured ten cases and reduced 15 to the no-further-treatment level, the mixed treatment needed 45 to cure 18 and bring seven to the no-further-treatment level whereas in the thymol group 80 treatments were needed to cure ten and bring 12 to the no-further-treatment level. In this last group one case left hospital after three and two cases after four treatments with egg counts of over 1,000 eggs

per c.cm., so that at least 83 treatments would have been necessary to bring all the cases to the same level as those of the other two groups. It must be recorded that 22 of the subsequent treatments in the thymol group were not with thymol because, in four cases after two treatments and in all the others requiring them after three treatments with thymol, one or other of the alternative forms of treatment were given. The same thing applies in the mixed treatment group where thymol was given in four and tetrachlorethylene in two supplementary treatments\*. In view of the greater efficiency of the other treatments, which has been demonstrated above, it is not considered likely that they were less effective than thymol would have been in these cases so the much greater number of treatments needed in this group can be taken as further evidence of the relative inactivity of thymol. The fact that in six out of 11 cases more worms were passed after a dose of tetrachlorethylene than had been passed previously after a third dose of thymol can be interpreted in one of two ways, either that these worms had become 'fast' to thymol or that it again shows the superiority of tetrachlorethylene.

### Discussion

In assessing our results it may be argued that we did not use 60 grains of thymol in a single case whereas we did use 4 c.cm. of tetrachlorethylene without exception. The reason we reduced the dose of thymol was not to decry its value but we were guided by the opinion of Ashford (than whom none had wider experience in its use) that for safety the dose of thymol must be carefully regulated. We were dealing with adults, but their weight was so much below the usually-accepted normal of 150 pounds that they had to be regarded as under age from the point of view of therapeutics, because this method of calculating dosage is now recognized as much more scientific than to use age in years, particularly in illiterate persons whose statement of their ages is often most unreliable. With regard to tetrachlorethylene we had our own experience of many years' use of the drug on human beings as well as our pharmacological work on cats which showed that the dose of 4 c.cm. is so far below the dangerous limit that it is not necessary to reduce the dose in adults however low their weight may be. In addition to our own experience a good deal of other evidence of the safety of tetrachlorethylene has now accumulated and so far the only case

\*The reason this was done is that we hold the view that after two or three ineffective treatments with a drug some hookworms appear to become resistant or 'fast' to it. This conclusion was arrived at some years ago when we were experimenting to see if we could reduce the dose and retain the efficiency of carbon tetrachloride, in the interests of safety. We found that after two or three ineffective doses of 1 c.cm. of this drug a full dose of 3 c.cm. appeared to be equally inefficient. As the research failed in its primary object this observation was never published.

reported of its apparent dangerous toxic effects is that of Kendrick (1929) in which the serious symptoms rapidly passed off. As it is now over ten years ago since this isolated case was reported and no similar ones have since been recorded it seems reasonable to look on it as unique and of no real importance as an argument against the safety of tetrachlorethylene. Therefore we consider if the necessity for safety (stressed by Lane in the quotation given from

recommended by the greatest authority on its use.  
 There are other factors also worthy of consideration. The cost of tetrachlorethylene is Rs. 2 per pound, or less for a large quantity, whereas thymol is Rs. 7 or more a pound\* and as the full dose of these drugs is practically the same the advantage of tetrachlorethylene in this respect needs no discussion. Further, the sodium bicarbonate and/or the lactose and the

Intensity distribution, shown by egg counts

Eggs per c.cm. of stool	Over 20,000	19,999 to 10,000	9,999 to 9,000	8,999 to 8,000	7,999 to 7,000	6,999 to 6,000	5,999 to 5,000	4,999 to 4,000	3,999 to 3,000	2,999 to 2,000	1,999 to 1,000	Under 1,000	Total
Thymol ..	5	4	0	0	2	1	1	1	3	3	3	2	25
Tetrachlorethylene	2	3	0	1	3	1	0	3	3	2	7	0	25
Mixed treatment	2	9	0	1	1	0	0	2	2	3	5	0	25

Cases given tetrachlorethylene alone; the dose in all instances was 4 c.cm.

Number	Egg count	WORMS PASSED AFTER FIRST TREATMENT		WORMS PASSED AFTER SECOND TREATMENT		TOTAL WORMS		Result	REMARKS
		Nec.	Anc.	Nec.	Anc.	Nec.	Anc.		
1	1,200	19	..	..	..	19	..	Cured	
2	1,300	16	..	..	..	16	..	"	
3	1,400	106	..	..	..	106	..	"	
4	3,800	81	..	..	..	81	..	"	
5	4,800	99	1	..	..	99	1	"	
6	1,000	14	16	..	..	14	16	"	
7	6,000	2	130	..	..	2	130	"	
8	3,700	..	20	..	..	..	20	"	
9	7,000	..	31	..	..	..	31	"	
10	1,400	70	..	..	..	70	..	Not cured	1 egg by D. C. F.
11	8,400	137	..	..	..	137	..	"	1 " " "
12	20,500	682	..	..	..	682	..	"	4 eggs " "
13	2,000	..	6 *	..	..	..	6	"	Count under 100
14	2,900	223	1	..	..	223	1	"	" " " 100
15	7,900	5	89	..	..	5	89	"	" " " 100
16	1,900	297	18	..	..	297	18	"	2 eggs by D. C. F.
17	3,300	11	8	..	..	11	8	"	2 " " "
18	16,400	114	29	..	..	114	29	"	4 " " "
19	1,200	..	6	..	..	..	6	"	1 egg " "
20	4,200	..	36	..	..	..	36	"	1 " " "
21	7,300	..	125	..	..	..	125	"	1 " " "
22	19,000	?	?	..	..	?	?	"	2 eggs " " (stool not saved).
23	4,600	26	..	18	..	44	..	Cured	
24	15,500	..	44	..	16	..	60	Not cured	2 eggs by D. C. F.
25	25,400	..	340	..	20	..	360	"	2 " " "

The cases in all the groups have been arranged in order according to the ease with which they were cured, therefore they also give a graphic representation of the results.  
 \* Instances in which some worms were too broken to be identified.

his writings at the beginning of this paper) is accepted, as it should be, tetrachlorethylene fully comes up to his demands, as it appears to be even safer than thymol and there appears to be no doubt about its greater efficiency, when the dose of thymol is kept within the limits

gelatin capsules are all to be added to the cost of thymol, and a third factor in increasing its expense is that a considerable amount of time  
 (Continued at foot of page 200)  
 \* These are pre-war prices in Calcutta.

## Cases given mixed treatment, tetrachlorethylene and oil of chenopodium

Num- ber	Egg count	1st treat- ment	WORMS PASSED		2nd treatment	WORMS PASSED		3rd treatment	WORMS PASSED		4th treatment	WORMS PASSED		5th treatment	WORMS PASSED		Result	REMARKS
			Nec.	Anc.		Nec.	Anc.		Nec.	Anc.		Nec.	Anc.		Nec.	Anc.		
1	2,000		22	..	..	..	..	..	..	..	..	..	..	..	..	..	Cured	
2	1,600		30	..	..	..	..	..	..	..	..	..	..	..	..	..	"	
3	1,600		27	..	..	..	..	..	..	..	..	..	..	..	..	..	"	
4	2,400		46	..	..	..	..	..	..	..	..	..	..	..	..	..	"	
5	7,300		49	..	..	..	..	..	..	..	..	..	..	..	..	..	"	
6	11,600		59	..	..	..	..	..	..	..	..	..	..	..	..	..	"	
7	1,900		147	..	..	..	..	..	..	..	..	..	..	..	..	..	"	
8	8,100		68	2	..	..	..	..	..	..	..	..	..	..	..	..	"	
9	1,300		84	29	..	..	..	..	..	..	..	..	..	..	..	..	"	
10	10,600		69	72	..	..	..	..	..	..	..	..	..	..	..	..	"	
11	11,400		24	24	..	..	..	..	..	..	..	..	..	..	..	..	"	
12	15,700		219	6	..	..	..	..	..	..	..	..	..	..	..	..	"	
13	3,400		10	139	..	..	..	..	..	..	..	..	..	..	..	..	"	Count under 100,
14	12,900		..	39	..	..	..	..	..	..	..	..	..	..	..	..	"	100.
15	12,800		..	..	..	..	..	..	..	..	..	..	..	..	..	..	"	100.
16	18,100		41	..	Repeat treatment.	..	..	..	..	..	..	..	..	..	..	..	Cured	
17	3,600		93	..	"	..	..	..	..	..	..	..	..	..	..	..	"	
18	47,700		6	400*	"	..	..	..	..	..	..	..	..	..	..	..	"	
19	23,700		..	25*	"	..	..	..	..	..	..	..	..	..	..	..	"	
20	4,200		..	37*	"	..	..	..	..	..	..	..	..	..	..	..	Not cured	1 egg by D. C. F.
21	16,900		1,155	13	"	26	2	Repeat treatment.	..	3	..	..	..	..	1,181	18	Cured	
22	2,700		..	3	"	..	..	"	..	4	..	..	..	..	..	7	Not cured	4 eggs "
23	2,800		2	32	"	..	..	"	..	..	Thymol grs. 49	..	..	..	2	32	Cured	
24	10,700		10	13	"	..	2	"	..	11	Thymol grs. 42 C.Cl. 4 c.c.	..	2	Repeat thymol. Repeat C.Cl.	10	28	Not cured	Count under 100.
25	4,900		..	384	"	..	5	Thymol grs. 56	..	..	..	..	21	..	..	415	"	100.

In all cases tetrachlorethylene 4 c.cm. and oil of chenopodium 1 c.cm.

*Cases given thymol*

Num- ber	Egg count	Weight in lb.	1st treat- ment in grains	WORMS PASSED		2nd treat- ment	WORMS PASSED		3rd treat- ment	WORMS PASSED		4th treat- ment	WORMS PASSED		5th treat- ment	WORMS PASSED		TOTAL WORMS	Result	REMARKS
				Nec.	Anc.		Nec.	Anc.		Nec.	Anc.		Nec.	Anc.		Nec.	Anc.			
1	1,600	76	30	33	3	..	..	..	..	..	..	..	..	..	..	..	33	3	Cured	2 eggs by D. C. F.
2	1,700	86	34	9	..	..	..	..	..	..	..	..	..	..	..	..	9	..	Not cured	3 " "
3	500	82	32	3	..	..	..	..	..	..	..	..	..	..	..	..	3	..	"	"
4	2,000	79	32	7	..	..	..	..	..	..	..	..	..	..	..	..	7	..	"	Count under 100.
5	900	121	48	2	..	Repeat thymol.	..	..	..	..	..	..	..	..	..	..	2	..	Cured	
6	2,800	112	45	185	..	"	15	..	..	..	..	..	..	..	..	..	200	..	"	
7	1,000	90	36	5	..	"	16	..	..	..	..	..	..	..	..	..	21	..	"	
8	12,400	112	45	425	..	"	..	..	..	..	..	..	..	..	..	..	425	..	Not cured	4 eggs by D. C. F.
9	3,300	96	38	21	..	"	6	..	..	..	..	..	..	..	..	..	27	..	"	2 " "
10	16,100	142	56	19	27	"	..	11	C <sub>2</sub> Cl <sub>4</sub>	..	..	..	..	..	..	..	19	40	"	3 " "
11	6,200	112	45	2	55	"	..	3	"	..	..	..	..	..	..	..	2	94	"	3 " "
12	25,000	87	35	76	30	"	..	2	Mixed	1	68	Mixed	..	38	..	..	77	138	"	Count 1,400 re- fused to stay.
13	5,000	125	50	1	15	"	..	11	C <sub>2</sub> Cl <sub>4</sub>	..	12	C <sub>2</sub> Cl <sub>4</sub>	..	2	..	..	1	40	Cured	
14	10,300	87	35	3	42*	"	..	13*	Repeat thymol.	..	..	"	..	13	..	..	3	68	"	
15	7,300	55	25	20	25	"	..	35	"	..	..	"	..	1	..	..	20	26	"	
16	2,000	84	34	..	2	"	..	7	"	..	9	"	..	11	..	..	..	57	"	
17	26,400	101	40	47	216	"	..	24	"	..	2	"	..	1	..	..	47	226	Not cured	Count under 100.
18	3,000	107	42	..	92	"	..	7	"	..	2	"	..	4	..	..	..	122	"	Count 1,100 re- fused to stay.
19	20,000	90	36	..	19*	"	..	..	"	..	2	"	..	11	..	..	..	39	"	Discharged (had leprosy).
20	39,600	93	36	..	7	"	11	17	"	..	9	"	..	..	..	..	11	33	"	
21	4,100	94	38	..	68	"	..	8	"	..	1	"	..	5	C <sub>2</sub> Cl <sub>4</sub>	1	..	83	Cured	
22	7,900	100	40	..	16	"	..	19	"	..	14	"	..	11	"	2	..	62	"	Count 100.
23	3,400	120	48	..	10	"	..	12	"	..	1	"	..	40	"	..	..	63	Not cured	"
24	16,400	85	34	3	149	"	..	30	"	..	2	"	..	..	"	..	3	181	"	100.
25	27,700	104	42	2	33	"	..	11	"	..	1	"	..	8	"	..	15	53	"	100.

# HAFFKININE (ACRIQUINE), AN ATEBRIN-LIKE COMPOUND PREPARED IN INDIA, IN INDIAN STRAINS OF MALARIA

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SINCE the discovery of the antimalarial properties of atebirin and its successful use in

(Continued from page 197)

of trained dispensers would be occupied in preparing a large number of doses. Against this, tetrachlorethylene requires no excipients nor capsules and it can be rapidly and accurately measured by anyone with ordinary intelligence but with no special training as a dispenser\*. A final advantage of tetrachlorethylene, according to our method of treatment, is that it is mixed directly with the dose of purgative, shaken up and given immediately in a single dose, whereas thymol is given in one or two portions, which are followed in an hour or two by the purgative, so that the time taken to complete the treatment with this drug is much greater than that occupied in giving tetrachlorethylene.

Accordingly our final conclusion is that tetrachlorethylene is a better drug for the treatment of hookworm infection on the grounds of lower toxicity, lower cost, greater ease of dispensing, less time taken in completing a treatment, and greater efficiency.

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\* An accurate and efficient measure for dispensing tetrachlorethylene is an old-fashioned type of hypodermic syringe of 5 c.cm. capacity, which has a screw-nut on the plunger-bar to limit the excursion of the plunger so that any desired amount of liquid less than 5 c.cm. in volume can be automatically measured. In the present instance the screw is adjusted so that only 4 c.cm. can be drawn into the syringe. Used without the needle attached, accurate doses can be measured in this way and expelled into already prepared doses of the purgative with the greatest rapidity.

the routine treatment of malaria, efforts have been made in other countries to prepare acridine derivatives of a similar nature and with similar properties. In France, 'quinacrine', a compound with the same constitutional chemical formula, was prepared and successfully tested, while in the Union of Soviet Socialist Republics 'acriquine' a similar compound was synthesized. A comparative study of the actions of these two compounds on malarial infections reveals no difference. They destroy all the stages of the three species of malarial parasites with the exception of the gametocytes of *P. falciparum*. Like atebirin these compounds are mainly excreted through the kidneys and traces of them were found in the urine for a considerable period.

Recently, workers in the Haffkine Institute, Parel, Bombay, have prepared a similar acridine derivative the therapeutic efficacy of which has been tested by us on a series of eight cases in the Carmichael Hospital for Tropical Diseases. The compound was at first called 'Haffkinine' but this name has now been changed to 'acriquine' and in this paper we have given the summary of results of these trials.

After the patients were admitted into the hospital a thorough physical examination was carried out; the peripheral blood was examined and a rough estimate of the number of parasites, both sexual and asexual, was also made. Except in urgent cases, the patients were put on a simple alkaline mixture and the antimalarial treatment was not started until the parasitic counts were fairly constant for two or three consecutive days. The pulse rate, blood pressure and respiration were recorded. Daily counts of parasites in the peripheral blood during this period enabled us to watch the progress of the patients and gave us information with regard to the intensity of the infection and the action of the drug. If parasites in the peripheral blood were scanty, these were allowed to increase till the count was fairly advanced, and rigors and other symptoms were pronounced before the drug was administered. 'Haffkinine' (acriquine) was given by the mouth in powder form, one tablet, containing 0.1 gramme, being given three times a day for five consecutive days. To two cases, however, it was administered in gelatine capsules. No other drug was given except a light purgative whenever necessary. No restrictions regarding diet were observed. Daily examinations of blood were carried out for malaria parasites during the course of treatment, and a rough estimate of the number of parasites was also made wherever possible.

After the completion of the course the patients were carefully observed in the hospital for a fortnight, daily examinations of the blood being made for malarial parasites. Cultural examinations of the blood for malarial parasites were made where thin and thick films were negative.

Details of eight cases are given in the table. A study of the table will show that the



TABLE

Number	Race, Sex and Age	FINDINGS OF PARASITES BEFORE TREATMENT			FINDINGS OF PARASITES DURING AND AFTER TREATMENT								Duration of fever in days after beginning of treatment	REMARKS
		Species	As.*	Sex.	2nd day		3rd day		4th day		5th day			
					As.	Sex.	As.	Sex.	As.	Sex.	As.	Sex.		
1	E., M., 38	MT	Sc.	0	0	0	0	0	0	0	0	0	1	Crescents persisted.
2	H., M., 30	BT & MT	1,000	0	1,000	0	200	Cr.	Sc.	Cr.	Sc.	Cr.	3	
3	O.C., M., 22	BT	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	0	0	0	0	3	1/3 the adult dose given for seven days. Asexual forms disappeared on the sixth day. Crescents persisted.
4	I.Ch., M., 3	MT	900	Sc.	500	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	4	
5	H., M., 20	MT	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	2	Induced malaria.
6	H., M., 32	MT	Sc.	0	Sc.	0	0	0	0	0	0	0		Temperature persisted, chronic cough.
7	O.C., F., 12	(Rings). MT	Sc.	0	Sc.	0	0	0	0	0	0	0	2	Drug given for four days. No relapse within six weeks.
8	H., M., 22	BT	1,750	450	650	350	950	225	Sc.	0	0	0	3	No relapse within nine weeks.

Note.—The figures given, indicate parasite per 500 leucocytes.

Sc. indicates 'scanty', i.e., less than 200 per 500 leucocytes.

Cr. indicates scanty crescents.

\* As. = Asexual forms.

temperature came down to normal within one to four days and the peripheral blood was free from parasites within two to five days. The drug destroys all the forms of malaria parasites excepting the gametocytes of *P. falciparum*. Its action closely resembles that of atebirin and other acridine derivatives. Unfortunately, we had no case of quartan infection in the hospital during the period of this investigation. Rigors were seldom observed on the third day of the administration of this drug. In mild cases of benign tertian infection, if treatment with this drug was started on the day of the rigor, the next rigor was sometimes manifested in the form of a chilly sensation only. The effects of the drug on blood pressure, pulse rate and respiration were recorded; no marked changes were noticed. Haffkinine (acriquine) was mostly excreted by the kidneys and appeared in the urine on the second day of its administration, and traces of it were detected up to 25 days or even longer. A slight yellow tinge, which passed off after a few days, developed in the skin of some of the cases. There was rapid reduction in the size of the spleen in cases of acute infection, but in long-standing cases where the spleen was hard the decrease in size was more gradual and the organ often took a considerably longer time to come back to its normal size. In spite of the fact that Haffkinine persisted in the body for a fairly long time, no marked untoward symptoms were noticed. One or two cases complained of slight pain or a sensation of uneasiness in the epigastric region and loss of appetite,

but these symptoms passed off with the stoppage of the medicine.

#### Summary and conclusions

(1) Haffkinine or 'acriquine', an acridine derivative prepared in India, is an effective drug in the treatment of Indian strains of malaria. The drug is effective in doses of 0.1 gramme three times a day, the course lasting for five days and taking a total of 1.5 grammes of the drug for the cure.

(2) Haffkinine (acriquine) in this small series of cases appeared to behave in the same way as atebirin would have done.

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CRINODORA (PALUSAN) IN INDIAN STRAINS OF MALARIA

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AFTER the synthesis and successful trials of atebtrin in the treatment of malaria, a number of acridine derivatives closely resembling it in chemical composition and properties were prepared. In France, 'quinacrine' was synthesized and in the U.S.S.R. 'acriquine'. Soon after, S. A. Farmaceutici Italia Milano synthesized a similar compound which they called 'Palusan' and later 'Crinodora', the chemical composition of which, as stated by the manufacturers, is the same as that of atebtrin. As the supplies of atebtrin in India from German sources have been stopped on account of the outbreak of war, we undertook to test this drug in the treatment of infections with Indian strains of malaria, so that, if the acridine derivatives prepared in Italy resembled atebtrin closely, use could be made of this source for the supply of another effective antimalarial drug in this country.

The investigation was carried out on a series of 44 patients in the Carmichael Hospital for Tropical Diseases. Most of the patients came from different parts of Bengal where malaria is endemic. The studies were mainly undertaken to determine : (a) the effects of the drug on the temperature and other symptoms; (b) its effects on the asexual and sexual forms of the parasites,

and the time taken for their disappearance from the peripheral blood; (c) its effect on the splenic enlargement; (d) the effect of the drug on the pulse rate, blood pressure, respiration, and generally on the patients, and its excretion from the body; (e) any untoward effects produced by its administration. In this paper the results of these trials are summarized.

On admission of patients a thorough physical examination was carried out; the peripheral blood was examined and a rough estimate of the number of parasites, both sexual and asexual, was made. Except in urgent cases, the patients were put on a simple alkaline mixture and the antimalarial treatment was not started until the parasite counts were observed for two or three consecutive days. This gave valuable information regarding the intensity of the infection. If the parasites in the peripheral blood were scanty, these were allowed to increase till the rigors and other symptoms were pronounced, and then the drug was administered. Crinodora (palusan) was given by the mouth in tablet form, one tablet, containing 0.1 gramme, being given three times a day for five consecutive days. No other drug was given except a mild purgative whenever necessary. No restrictions regarding diet were observed. Daily examinations of the blood were carried out for malaria parasites during the course of treatment and a rough estimate of the number of parasites was also made wherever possible. The pulse, blood pressure and respiration were carefully recorded.

After completion of the course the patients were kept in hospital for a fortnight, daily examinations of the blood for parasites being made during this period. Cultural examinations of the blood for malarial parasites were also made where thin and thick films were negative.

TABLE

Race, Sex and Age	Species	FINDINGS OF PARASITES BEFORE TREATMENT PER 500 LEUCOCYTES		FINDINGS OF PARASITES DURING AND AFTER TREATMENT. PARASITES PER 500 LEUCOCYTES								Days of fever after beginning treatment	REMARKS	
		As.*	Sex.	2nd day		3rd day		4th day		5th day				
				As.	Sex.	As.	Sex.	As.	Sex.	As.	Sex.			
H., M., 22	B T	240	Sc.	200	Sc.	Sc.	0	0	0	0	0	0	2	H. W. Total dose 1 g. Parasites free next day.
H., M., 23	B T	Sc.	0	Sc.	0	0	0	0	0	0	0	0	2	
H., F., 5	B T and MT	350	Sc. (B T)	275	Sc. (B T)	Sc.	0	0	0	0	0	0	2	
H., M., 25	B T	Sc.	Sc.	Sc.	Sc.	0	0	0	0	0	0	0	2	
H., M., 12	B T and B T	508 (M T and B T)	0	316 (M T and B T)	0	220 (M T and B T)	0	128 (M T and B T)	0	Sc. (M T and B T)	0	0	4	
M., M., 62	Q T	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	4	Parasites free next day.

TABLE—concl'd.

Race, Sex and Age	Species	FINDINGS OF PARASITES BEFORE TREATMENT PER 500 LEUCOCYTES		FINDINGS OF PARASITES DURING AND AFTER TREATMENT. PARASITES PER 500 LEUCOCYTES								Days of fever after beginning treatment	REMARKS	
		As.*	Sex.	2nd day		3rd day		4th day		5th day				
				As.	Sex.	As.	Sex.	As.	Sex.	As.	Sex.			
H., M., 32	M T	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	0	Sc.	0	Sc.	3	Crescents killed by plasmochin.	
H., M., 25	B T	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	1		
H., M., 24	B T	410	Sc.	225	Sc.	Sc.	0	0	0	0	0	2		
H., F., 22	M T	525	0	325	0	110	0	Sc.	0	0	0	3		
A.-I., F., 60	M T	425	0	212	0	110	Sc.	Sc.	Sc.	0	Sc.	3	Crescents persisted. Pains slight in epigastrium. Crescent persisted.	
H., M., 40	M T	325	0	Sc.	0	Sc.	0	0	0	0	0	1		
M., M., 38	M T	625	Sc.	450	Sc.	175	Sc.	Sc.	Sc.	0	0	3		
H., M., 33	B T	Sc.	Sc.	Sc.	Sc.	0	0	0	0	0	0	1		
H., M., 17	M T	495	0	329	Sc.	128	Sc.	Sc.	Sc.	0	Sc.	3	Do.	
H., M., 41	B T	Sc.	0	Sc.	Sc.	0	0	0	0	0	0	0		
H., M., 49	M T	320	0	130	0	Sc.	0	0	0	0	0	1		
M., M., 52	B T	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	1		
H., M., 15	B T	595	0	320	0	300	0	124	0	Sc.	0	3	Parasite free following day.	
A.-I., M., 34	M T	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	1		
M., M., 44	M T	398	0	198	0	118	0	Sc.	0	0	0	2		
H., M., 47	M T	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	1		
M., M., 20	B T	275	Sc.	150	Sc.	Sc.	0	0	0	0	0	..	Crescents disappeared spontaneously after three weeks.	
H., M., 45	M T	317	0	300	0	150	Sc.	Sc.	Sc.	0	Sc.	..		
H., M., 30	M T	Sc.	0	0	0	0	0	0	0	0	0	..		
I.Ch., M., 25	B T	425	100	250	90	300	Sc.	Sc.	Sc.	0	0	..		
M., M., 20	M T	320	Sc.	180	Sc.	80	Sc.	Sc.	Sc.	0	Sc.	..	Apyrexial	H. W. Colitis. Anæmia.
H., M., 31	M T	Sc.	0	Sc.	0	0	0	0	0	0	0	..		
H., M., 50	B T	310	0	200	0	110	0	Sc.	0	0	0	..		
I.Ch., M., 15	M T	650	Sc.	275	Sc.	Sc.	Sc.	0	Sc.	0	Sc.	..		
H., M., 33	B T	Sc.	Sc.	Sc.	Sc.	0	0	0	0	0	0	3	Parasite free next day. 1.8 g. given. Parasite free 6th day.	
I.Ch., M., 30	B T	780	Sc.	310	Sc.	Sc.	Sc.	0	0	0	0	2		
H., M., 1	B T	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	0	0	4		
M., M., 24	M T	340	0	200	0	85	0	130	0	Sc.	0	4		
A.-I., M., 37	M T	258	0	150	0	Sc.	0	Sc.	0	Sc.	0	4	? Blackwater fever. 2.1 g. given. History of hæmaturia. Parasite free 6th day.	
H., M., 47	B T	374	Sc.	205	0	Sc.	0	Sc.	0	0	0	3		
H., M., 19	B T	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	2		
M., M., 28	M T	278	0	190	0	Sc.	0	Sc.	0	0	0	3		
H., M., 30	M T	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	2		
A.-I., F., 46	M T	421	0	318	0	116	0	Sc.	0	0	0	3		
M., M., 37	B T	Sc.	0	Sc.	0	Sc.	0	0	0	0	0	3		
H., M., 32	M T	Sc.	0	0	0	0	0	0	0	0	0	2		
A.-I., M., 45	M T	Sc.	0	Sc.	0	Sc.	0	Sc.	0	0	0	3		
A.-I., 48	Q T	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	Sc.	4		

\* As. = Asexual forms.

Details of 44 cases are given in the table. A study of the table will show that the temperature in all the three species of parasites usually

begins to settle down after 0.6 gramme to 0.9 gramme of the drug has been administered and there is complete disappearance of the parasites

from the peripheral blood after 0.9 gramme to 1.2 gramme, except in quartan infections, where the drug had to be given for two more days to make the blood parasite-free. The drug has no action on the gametocytes of *P. falciparum*.

Rigors are seldom observed after the third day of administration of 'crinodora'. In mild cases of benign tertian infections, if the treatment with 'crinodora' is started on the day of the rigor, the next rigor is sometimes manifested in the form of a chilly sensation only, and in cases infected with the quartan type it does not come at all.

The blood pressure, pulse rate and respiration were recorded. So far as the blood pressure is concerned, there was a slight lowering, varying from 8 to 12 millimetres of mercury in some patients. In others there was no change whatsoever. The pulse rate and respiration also showed no appreciable changes when the patients were under the effect of the drug. From these results one is justified in concluding that 'crinodora' has little if any depressing effect on the cardiovascular system in the majority of the patients.

**Excretion.**—In a series of patients we worked out the excretion of this compound. It is mostly excreted by the kidneys and appears in the urine on the second day after administration and can be detected up to 25 days or longer. Three patients under treatment with 'crinodora' developed a slight yellow colour in the skin which passed away after a few days.

**Splenic enlargement.**—There was rapid reduction in the size of the spleen to practically its normal size in every case of acute infection, but in long-standing cases, where the spleen was hard, the decrease in size was more gradual and the organ often took a considerable time to come back to its normal size.

**Untoward and toxic effects.**—In spite of the fact that 'crinodora' persists in the body for a fairly long time no marked untoward symptoms were noticed. One or two cases complained of slight pain or a sensation of uneasiness in the epigastric region. A few of our patients have occasionally complained of loss of appetite while the drug was being given, but the condition passed off with the discontinuance of the medicine.

#### Summary and conclusions

(1) 'Crinodora (palusan)' is an effective drug in the treatment of Indian strains of malaria. It is usually effective in doses of 0.1 gramme three times a day, the course lasting for five days and making a total of 1.5 gramme of the drug for the cure. The drug has no action on crescents.

(2) The drug behaves in exactly the same way as atebrin and would make an excellent substitute for it now that the supplies from Germany have been cut off.

## IDIOPATHIC HYPOCHROMIC ANÆMIA WITH A CASE NOTE

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IDIOPATHIC hypochromic anæmia is a chronic form of anæmia found mostly in middle-aged women; it is associated with epithelial changes in the tongue and in the nails.

**Ætiology.**—Over 96 per cent of cases occur in women (Wintrobe and Beebe, 1933) and the maximal incidence is between the ages of forty and fifty; the condition is rare below twenty and uncommon above fifty. Repeated pregnancy, as well as excessive loss through menstruation, are responsible for a large number of cases (Davidson *et al.*, 1935).

From experimental evidence Heath, Strauss and Castle (1932) conclude that the main cause of the disease is iron deficiency. In a woman this may be due to a continual drain on the iron reserve of the body during the period of sexual life, deficient intake, and failure of proper absorption on account of hypochlorhydria or achlorhydria, iron being more readily absorbed from an acid medium (Mettier and Minot, 1931).

Although hypochlorhydria or achlorhydria is comparatively more common in women than in men (Davies and Shelley, 1934), they are not infrequently seen in men, whereas idiopathic hypochromic anæmia is rarely seen in men. It is therefore presumed that the low gastric acidity is not the main cause of the anæmia and that it is probably associated with some other, as yet unknown, deficiency of gastric secretion.

**Symptomatology.**—In addition to the physical signs and symptoms which accompany anæmia, remarkable epithelial changes are common. Epithelial atrophy of the upper part of the alimentary tract is the most frequent finding; the tongue is denuded of papillæ and is often sore and there may be painful fissures at the angles of the mouth.

Occasionally, there is atrophy of the pharyngeal mucosa, which when associated with dysphagia constitutes the Plummer-Vinson syndrome. Mucosal atrophy of the stomach is present in a number of cases and may be seen by means of the gastroscope; this is probably the basis of the hypochlorhydria or achlorhydria which is reported in a large number of cases (Witts, 1931; Davies, 1931; Mills, 1931; Oliver and Wilkinson, 1933). Gastro-intestinal symptoms, such as abdominal pain, anorexia, eructations, a sensation of fullness even after small meals, nausea, and vomiting, are usually present and are probably due to lack of an adequate amount of hydrochloric acid and an excess of mucus which makes the gastric juice very viscid (Davies, *loc. cit.*).

In addition to these changes in the gastro-intestinal tract, alterations in the nails are

common. They become more brittle with a tendency to split longitudinally, tender, flat and sometimes actually spoon-shaped, i.e., koilonychia.

The hair is dry and scanty, and the patient is usually of a nervous and worrying temperament. Numbness and tingling in the limbs may be present, but definite organic nervous lesions are absent (Witts, 1930; Wintrobe and Beebe, 1933). Slight enlargement of the spleen is found in about 60 per cent of cases if the anæmia is marked, but the enlargement is seldom of any considerable degree (Witts, 1930). Loss of blood through menstruation may be excessive but becomes normal after efficient treatment.

**Hæmatology.**—The anæmia is definitely hypochromic and microcytic. The red cell count lies between 3 to 4 millions per c. mm., whilst the average hæmoglobin is below 6 grammes per 100 c.cm. The following figures given by Wintrobe and Beebe (1933) are on the average of 25 cases :—

Volume of packed red cells—29.5 c.cm. (limits 16.8 to 38 c.cm.).

Mean corpuscular volume—65 cu.  $\mu$  (limits 65–74 cu.  $\mu$ ).

Mean corpuscular hæmoglobin—18  $\gamma\gamma$  (limits 15–21  $\gamma\gamma$ ).

Mean corp. hæmoglobin concentration—27 per cent (limits 25–30 per cent).

Anisocytosis and poikilocytosis may be present, but are not marked. Normoblasts may be found in cases of severe anæmia, and the reticulocytes are within normal limits. The mean red cell diameter is from 6.2 to 6.7  $\mu$ , and the Price-Jones curve has a broad base with the peak on the left and the range of microcytosis is from 6 to 37 per cent (Price-Jones, 1932).

The total and differential leucocytic count is generally within the normal limits, but Witts (1930) describes a group of cases in which leucopenia was observed. The platelets, the coagulation time, the bleeding time, and the fragility of red cells are all within normal limits. The direct van den Bergh test is negative and the indirect test is also well within the normal range. There is no excess of urobilin in the urine.

**Gastric analysis.**—Hypochlorhydria or achlorhydria was found to be present in over 80 per cent of cases by Witts (1931) and Davies (1931) and by Oliver and Wilkinson (1933) in over 50 per cent of cases even after histamine, whereas Vaughan (1936) found achlorhydria in only 14 per cent of cases. Though Davies (1931) found achlorhydria in a large number of cases, according to him achlorhydria in idiopathic hypochromic anæmia is only 'apparent' or 'relative' and is not absolute as in pernicious anæmia. The above view is supported by

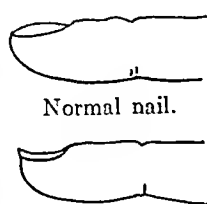


Fig. 1.

Meulengracht (1932) who holds that 'the achylia is not of the same radical character as in pernicious anæmia and in a few cases it may be designated more correctly as hypochylia'.

**Sternal puncture.**—The bone marrow obtained by sternal biopsy shows hyperplasia of the red cell elements with a very large number, generally over 40 per cent, of normoblasts in the different counts.

### Differential diagnosis

**Pernicious anæmia.**—The characteristic clinical picture, the macrocytic hyperchromic blood picture with a megaloblastic reaction of the marrow, and achylia of the gastric juice, all serve to distinguish it very clearly from idiopathic hypochromic anæmia.

**Splenic anæmia.**—This is seen in young adults, the spleen is greatly enlarged, there is persistent leucopenia which is due to neutropenia and hæmatemesis is common.

**Aplastic anæmia.**—All the formed elements of the blood including the white blood cells and the platelets are diminished, the volumetric determinations are normal, and the anæmia is normocytic, orthochromic, while the sternal biopsy shows an aplastic marrow.

**Malignant disease.**—Chronic loss of blood from the gastro-intestinal tract should be excluded by careful examination of the stools for occult blood. In these cases the anæmia responds to a certain extent to iron treatment, but only to reappear when the iron therapy is withdrawn.

### Treatment

The only efficient treatment lies in giving iron in large doses over long periods. The oral route is a far better method of administration than parenteral injection, although 1,000 milligrammes of iron and ammonium citrate by mouth is said to be equivalent to 32 milligrammes of iron given by intra-muscular injection (Heath, Strauss, and Castle, 1932) and although there may be digestive disturbances, and failure of adequate absorption in the absence of any free hydrochloric acid in the stomach. Administration of iron by parenteral injection is painful and an adequate dose can never be given without unpleasant toxic symptoms (Witts, 1931). But with the large doses which are now given by mouth adequate absorption is ensured and ample margin for waste is allowed. Constipation, which was at one time thought to be inevitable, is actually rare, and on the contrary diarrhoea may occur for the first few days.

By the oral route, inorganic iron preparations are superior to the organic; for relative potency the more commonly used preparations are placed in the following order (Witts, 1933) :—

Ferrous salts; scale preparations; ferric salts; organic compounds.

The minimum effective dose is ferrous sulphate 12 grains a day, Blaud's pill 45 grains a day, or iron and ammonium citrate 60 to 120 grains

a day. Ferrous salts should always be given in powder or tablet form, for when kept in liquid form they soon oxidize to ferric salts. The iron by mouth should be given for 3 to 4 weeks, and if necessary a second or third course with a short interval in between the courses may be given without any bad effect. In most cases, the result of treatment is dramatic and with adequate dose there is a gain of 0.3 gramme of hæmoglobin a day.

Hydrochloric acid in doses of half to one drachm should be given with the iron, in cases of hypochlorhydria or achlorhydria. It is a good appetizer, relieves dyspepsia, and promotes absorption of iron.

**Copper.**—The opinion on the value of copper is conflicting, but for all practical purposes all iron preparations contain quite enough copper as an impurity, and there is no need to give it separately.

**Liver.**—Whole liver contains a certain amount of iron and it is on account of this that generally there is a sense of well-being and some improvement after liver treatment, but the improvement is never sustained. And on the whole, liver extracts, stomach preparations, and proprietary preparations said to contain hæmoglobin, besides being expensive, are useless in the treatment of idiopathic hypochromic anæmia.

**Blood transfusion.**—This should be used only in very extreme cases to tide over the critical condition whilst the iron has time to take effect.

### Complications

Any septic foci that may exist should be attended to as soon as the patient is somewhat improved, for they reduce the efficiency of iron therapy and a permanent cure may never be effected in the presence of a septic focus.

### Pathology

Pathological evidence is rather scanty as patients rarely die of the disease. The pathological changes found in the various organs are those of chronic anæmia and depend on the severity of the anæmia. The bone-marrow is hyperplastic and is crowded with macro-normoblasts and normoblasts which may constitute over 50 per cent of the total cells. It indicates that there is some maturation defect at the normoblastic level, the formation of the red cells proceeds up to the normoblastic level, but these, in the absence of adequate amount of iron, fail to mature properly, consequently the marrow is over-crowded with normoblasts and the cells that enter the circulation are smaller in size and do not contain the full amount of hæmoglobin.

The mucosa of the tongue and of the pharynx is usually atrophied and may be ulcerated; sometimes atrophy of the mucosa of the stomach also may be seen.

### Case note

Mrs. Z., a European, aged 45, was admitted into the Carmichael Hospital for Tropical Diseases on 8th May.

1939, for anæmia. The patient had been treated in this hospital about one year ago for gastro-intestinal trouble. Examination at that time did not show anything excepting a certain amount of visceroptosis (revealed by a barium meal) for which she was advised an abdominal belt. For the last three months she had not been well. There had been a gradual increase in weakness—she was easily tired, and had palpitations on slight exertion. She suffered from headache, mostly in the afternoons and had no inclination for food or drink, and suffered from nausea and flatulent dyspepsia, even after small meals, for which reason she was very reluctant to take any nourishment.

**Examination of the patient.**—The patient was fairly well nourished, with a sallow complexion, mouse-coloured hair turning grey, and an increase in pigmentation on the face.

There was slight puffiness of the face, but no œdema of the feet. The tongue was small, denuded of papillæ, and slightly sore. The finger nails were tender and showed striking changes—they were brittle, flat, spoon-shaped with a tendency to split longitudinally, i.e., koilonychia. The teeth were bad, four of them being very loose.

**Abdomen.**—There was slight distension, the spleen and liver were not enlarged, there was no tenderness, and no mass could be felt on palpation.

**Circulatory system.**—No enlargement of the heart was noticed on percussion, but a hæmic bruit was heard over the mitral area. The respiratory system did not show any abnormality.

**Nervous system.**—The reflexes were normal, and except for the nervous and worrying temperament there was no other neurological symptom.

**Genito-urinary system.**—Menstruation was regular but scanty; urine was normal.

**Coagulation time.**—2 min. 45 secs. (capillary-tube method). Starting hæmolysis at 0.4 per cent of salt.

**Fragility of red cells.**—Complete hæmolysis at 0.3 per cent of salt.

**Wassermann reaction.**—Negative.

**Price-Jones curve.**—Mean diameter, 6.65 (see figure 2).

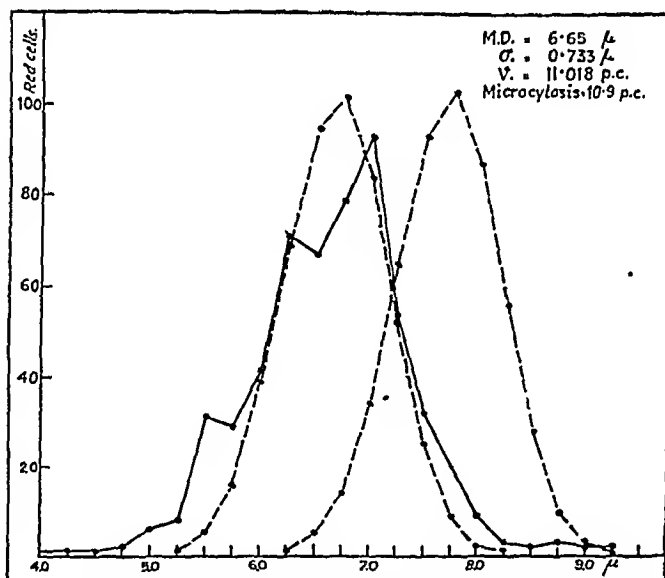


Fig. 2.—Red cell distribution curve of case reported with maximum and minimum ideal curves.

**Sternal puncture.**—This showed a hyperplastic marrow with more than 43 per cent normoblasts in the differential count of the nucleated cells.

**Fractional gastric analysis.**—Free hydrochloric acid was present within the normal limits and the fasting juice showed complete peptic digestion.

**Stool.**—No protozoa nor ova were found.

The test for occult blood was negative.

**Diagnosis.**—The case was diagnosed as one of idiopathic hypochromic anæmia.



## Laboratory examination

Date	Hæmoglobin in grammes per 100 c.cm.	Rcd blood cells in million per c.mm.	Reticulocytes per cent	Cell volume per cent	Mean corpuscular volume in cu. $\mu$	Mean corpuscular hæmoglobin in $\gamma\gamma$	Mean corpuscular hæmoglobin concentration per cent	White blood corpuscles per c.mm.	Neutrophils per c.mm.	Lymphocytes per c.mm.	Mononuclears per c.mm.	Eosinophils per c.mm.	van den Bergh mgm. per cent
8-5-39	6.32	3.69	1.0	24.0	65.0	17.1	26.3	6,450	4,800	1,024	384	192	neg.
26-5-39	9.92	4.33	6.3	35.0	80.7	22.9	28.3	..	..	..	..	..	0.4
2-6-39	11.68	4.36	3.0	37.0	84.6	26.7	31.6	6,250	..	..	..	..	0.2
13-6-39	13.37	4.14	0.1	40.0	96.6	32.2	33.3	..	..	..	..	..	neg.
29-6-39	14.02	4.85	0.4	42.5	87.2	28.8	33.0	7,300	..	..	..	..	neg.
24-8-39	14.57	4.76	0.2	46.0	96.6	30.6	31.6	8,650	..	..	..	..	neg.

## Treatment

The patient was at first put on ferrous sulphate gr. 6 three times a day—the routine method of iron therapy in our hospital. This increased her nausea and dyspepsia. So after three days, plastule (plain)\* was substituted for ferrous sulphate and these were given three times a day for a period of 42 days from 16th May to 26th June.

Seven teeth were extracted in stages, and the remaining teeth were scraped and cleaned.

*Progress.*—The patient showed definite signs of improvement from the first week of treatment. She gained about 2 grammes of hæmoglobin per week for the first three weeks of treatment with plastules—the maximum rise that one could expect with any efficient iron therapy. At the end of the treatment the blood picture had almost reached the normal level and the gastro-intestinal symptoms disappeared, koilonychia was fast disappearing and the patient had gained six pounds in weight.

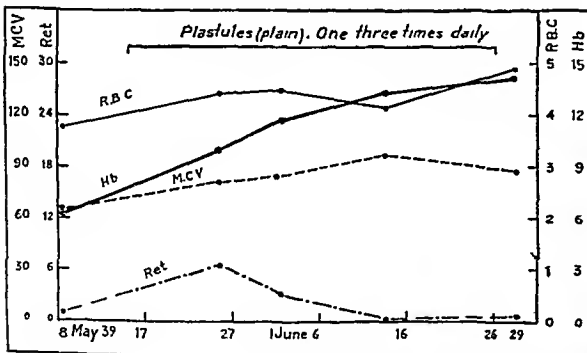


Figure 3

During the next two months, during which time no treatment had been given, the patient continued in perfect health, the finger nails were absolutely normal, and the blood picture was at the normal level.

\* Plastule (plain) is an iron preparation manufactured by John Wyeth and Brother, Limited. Each plastule (plain) contains ferrous sulphate, 5 grs., and dried yeast, 3/4 gr.; a liberal supply of plastule was given to us for trial by Mr. S. C. Chatterjee, a representative of the firm.

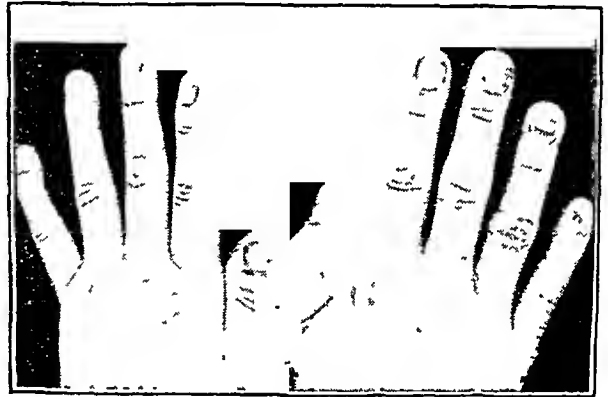


Fig. 4.—Nails showing koilonychia before treatment



Fig. 5.—Nails almost normal after treatment.

## Conclusion

A case of idiopathic hypochromic anæmia with typical koilonychia is reported; the condition responded to plastules (plain) in an orthodox manner.

Iron deficiency anæmia associated with koilonychia is a common finding in western countries. It has been reported by others in this country (Chaudhuri and Mangalik, 1938),

(Continued at foot of next page)

# TYPHUS FEVER IN BOMBAY

By T. B. PATEL, M.B., B.S., B.Sc., B.Hy. (Bom.),  
D.P.H. (Eng.)

(The City Fever Hospital Laboratory, Arthur Road,  
Bombay)

THE number of admissions to this hospital of suspected cases of enteric fever have very considerably increased since 1937.

TABLE I

FROM THE ANNUAL REPORTS OF THE EXECUTIVE HEALTH OFFICER, BOMBAY			FROM THE ANNUAL REPORTS OF THE MEDICAL SUPERINTENDENT, CITY FEVER HOSPITALS, BOMBAY	
Year	Registered cases		Admissions for	
	Enteric	Typhus	Enteric	Typhus
1932	308	1	3	0
1933	349	1	8	0
1934	341	0	32	0
1935	326	0	3	0
1936	387	0	8	0
1937	556	1	106	0
1938	1,168	0	235	0

(Continued from previous page)

but this is the first time that we have found a case with typical koilonychia though we have seen a large number of cases of iron deficiency anæmia.

## Acknowledgments

My thanks are due to Dr. L. E. Napier, under whose charge the patient was in hospital, for permission to report this case.

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From the beginning of June (1939) facilities for undertaking systematic laboratory investigation on cases of enteric fever became available and in consequence I have submitted every case of suspected enteric for close investigation. In cases where blood cultures and Widal tests proved negative, repeated tests were carried out on these cases for the typhus group and for undulant fever. In order that my findings may be controlled by a standard laboratory, I have uniformly employed, for diagnosis of enteric infections, typhus group of fevers and undulant fever by agglutination tests, standard antigens which have been supplied by the Enteric Laboratory, Kasauli.

The history and some of the clinical features of the seven cases hitherto diagnosed, with laboratory findings, are detailed below.

No case in this series showed a rash. All the patients were from the working classes.

Blood sera of cases 1, 4 and 5 were sent to Kasauli and blood sera of cases 4 and 5 were sent to the Hafikine Institute at the request of the Executive Health Officer, Bombay. These laboratories confirmed the diagnosis of typhus fever and obtained very much higher titres than mine. Although case 3 gave a low agglutination of 1:40 for OX19, it was undoubtedly a mild case of typhus from its clinical signs and symptoms.

## Treatment

In addition to the usual lines of treatment, cases 2, 5 and 6 were also given sulpha-pyridine compound (M. & B. 693) in doses of 2½ grammes per day for 5 to 7 days, as these cases were found to be very toxic. In these three the results obtained with the drug were promising. All the patients recovered.

## Summary and conclusions

1. The features common to all these cases are the predominance of pneumonic signs, severe pains all over the body, absence of rash, and their incidence mostly within the city municipal limits. Some degree of anæmia with prostration was also observed.

2. The occurrence of cases of endemic typhus fever in Bombay is definitely established.

3. The disease would have been more often diagnosed if all cases of continuous fever were serologically tested by the Weil-Felix reaction along with the Widal test.

4. Sulpha-pyridine (M. & B. 693) has been found to be of value in the treatment of this disease.

I take this opportunity to thank the officer in charge of the Enteric Laboratory, Kasauli, for his ready and prompt supply of the standard antigens and for his help in confirming some of my results, to Dr. B. P. B. Naidu for his co-operation in this study, and to the Medical

TABLE II

Number	Admitted on	Duration of illness	Sex	Age	Caste	Locality	Clinical features
1	3-6-39	12 days	M.	38	M.	Dadar	Marked toxæmia; cough; glossitis; temperature to normal by lysis on 10th day of admission.
2	16-6-39	16 "	M.	40	H.	Parel	Headache; cough; intense toxæmia; blood-shot eyes; pneumonia; temperature to normal by lysis on 11th day of admission.
3	5-7-39	8 "	M.	30	Ch.	Andheri	Slight toxæmia; tongue heavily coated; spleen palpable; temperature to normal by lysis on 8th day of admission.
4	25-7-39	11 "	M.	22	H.	Tardeo	Tongue raw at the tip and coated elsewhere; pneumonia; spleen palpable; anæmia; temperature to normal by lysis on 8th day of admission.
5	30-7-39	8 "	M.	30	M.	Nulbazar	Broncho-pneumonia; very toxic; developed later marked anæmia; temperature to normal by lysis on 8th day of admission.
6	6-9-39	4 "	M.	20	H.	Walkeshwar	Pneumonia; spleen palpable; toxæmia marked; abdominal distension; temperature to normal on 6th day of admission.
7	25-11-39	4 "	M.	30	M.	Nagpada	Severe joint pains; moderate toxæmia; slow pulse; bronchitis; temperature to normal by lysis on 7th day of admission.

TABLE III

Results of the Weil-Felix reaction—agglutination tests were put up to a titre of 1 : 320 only

Case	Date	Widal test	WEIL-FELIX TEST			B. abortus
			OX19	OX2	OXK	
1	20-6	—	1 : 320	—	—	—
	23-6	—	1 : 320	1 : 320	—	—
2	23-6	—	1 : 80	—	—	—
	28-6	—	1 : 80	—	—	—
	3-7	—	1 : 320	—	—	—
	7-7	—	1 : 80	—	—	—
	10-7	—	—	—	—	—
3	6-7	—	1 : 40	—	—	—
	9-7	—	1 : 40	—	—	—
	27-7	—	1 : 40	—	—	—
4	4-8	—	1 : 160	—	—	—
	7-8	—	1 : 320	—	—	—
	12-8	—	1 : 320	—	—	—
5	2-8	—	1 : 80	—	—	—
	6-8	—	1 : 320	1 : 20	—	—
	11-8	—	1 : 80	—	—	—
6	12-9	—	1 : 160	—	—	—
	14-9	—	1 : 320	—	—	—
	18-9	—	1 : 160	—	—	—
*7	30-11	—	1 : 320	1 : 40	—	—
	4-12	—	1 : 320	1 : 320	—	—

\* This case is still under treatment in the hospital.

Superintendent, Dr. P. T. Patel, of City Fever Hospitals, for his permission to publish these notes.

[Note.—The evidence that case 3 was typhus appears to be very slender: an agglutination (with OX19) of 1 : 40 is surely not significant especially in view of its constancy, and there seems to be nothing very specific in the clinical notes.

The treatment with M. & B. 693 the writer describes as 'promising', but the evidence that the three patients treated with this drug did any better than the rest seems to be lacking.—*Error, I. M. G.J*

## MINIATURE MASS RADIOGRAPHY\*

(A PLEA FOR ITS ADOPTION)

By SUDHIR C. ROY, M.B.

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THE method was first discussed in England and America within a short time of Röntgen's discovery of the  $x$ -rays, but the credit of introducing it in practice goes to Collender, who worked at it in South Africa for the first time in 1927 (Dormer and Collender, 1939). Independently of him, research along similar lines was undertaken in South America, Japan and Germany. To Janker (*Lancet*, 1939) belongs the credit of popularizing 'it in the last-named country, and as a result of the routine adoption in the Berlin Police Force, the morbidity from tuberculous disease of the lungs in the force has been brought down to almost the vanishing point.

The principle consists in photographing the image produced by the  $x$ -rays on the fluorescent screen. The essential requirements are a camera with a large aperture, a fluorescent screen and a film of fine grain. The exposure to the rays must be of short duration (not exceeding 1/20th second) with low penetration. In Germany an ordinary camera with roll-films was used with satisfactory results.

The position of the camera with regard to the fluorescent screen having been determined, it is fitted to the narrow end of a lead-lined funnel, whose broad end is fixed to the fluorescent screen. The funnel serves to exclude external light. The distance between the camera and

\* Read at a clinical meeting of the Barisal Branch of the Indian Medical Association.

the screen is approximately four feet, and had to be determined by the pioneers by a method of trial and error. The height of the combination should be adjusted according to the height of the patient. The x-ray tube is placed at a fixed distance at the screen-end of the funnel, and should also be adjustable.

The patient stands with his chest against the screen, and the exposure is taken after adjusting the tube to the centre of the screen. A reduced photograph of the image on the screen is taken by the camera, which is re-charged for the next patient, with a special device. The film in the camera can be made to turn-on automatically with the action of the exposure-switch.

The films are developed in the ordinary way, and are later read under a magnifier or in a projector, or the prints may be enlarged on bromide paper to any required size.

In a plant for extensive miniature radiography, the parts must be made for 'heavy duty', should have 'adequate' protecting arrangements and a rapid cooling device for the tube. With such a plant, an operator can 'at reasonable estimate' examine 100 patients in an hour. It has been calculated that the cost amounts to only a penny per case.

Collender used a single tube, which he cooled by immersing in circulating oil. Janker (*loc. cit.*) simplified the process by using two tubes mounted on a single pillar. When one of the tubes became heated it was replaced by the other. Recently Dormer and Gibson (1939) have used a double set of appliances and operators, and have immensely facilitated the work. Using two Rotalix tubes with a single generator and a rapid change-over arrangement, they have eliminated the loss of time taken in preparing a patient for exposure. Two operators working five hours a day have been able to take 600 exposures with this arrangement.

The optimal size of the radiogram is 24 mm. square, and the details are clearly exhibited for diagnostic purposes. In bromide enlargement of the reprints, the details are to some extent lost but are still comparable. Compared with the results of routine screen-examination, it has been found to be more reliable. Moreover, a permanent record of the condition remains.

Now that enquiry into the problem of pulmonary tuberculosis (especially mass surveys) has become popular in different parts of the country, and that the unique importance of chest radiography in the condition has been well recognized, the introduction of miniature mass radiography as a routine measure is all the more desirable, especially in a country such as India where economic considerations rank first. Moreover, the rapidity with which such radiographic examinations are possible is an additional advantage in examining large groups of students, factory and office workers and recruits for the militia. Its use may also be extended to serial

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## ROLE OF X-RAY SCREENING IN DETECTING PULMONARY TUBERCULOSIS\*

By K. EISENSTAEDT, M.D., T.D.D.

and

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REGARDING the various branches of the anti-tuberculosis campaigns carried on in recent times, such as treatment, prevention, after-care, etc., we have to bear in mind that the diagnosis is of primary importance. It goes without saying that best results depend on early detection. For

\* Read before the meeting of the Nawanagar Medical Society, on 13th December, 1939, at Jamnagar.

(Continued from previous column)

recording in artificial pneumothorax and other forms of collapse therapy.

In the western countries, Germany, America and England, the importance of miniature radiography has been enhanced as a result of its possibilities in examining recruits for the army. In times of war-emergency this rapid method of medical examination of the recruits has the double advantage of combining cheapness with rapidity, and miniature radiography, though not ideal, gives results sufficient for inclusion as a routine method for every case. Moreover, the chances of affected individuals escaping detection and passing into the ranks are negligible. In fact, the recent death of a militiaman from pulmonary tuberculosis within a few weeks of being classed as grade 1 by a medical board, has focussed attention on the importance of radiological examination of recruits. Miniature radiography has been suggested as the means of obviating such incidents in future.

At present in the tuberculosis survey, undertaken by the Bengal Public Health Department, at Barisal, a sum of Rs. 6,000 has been allotted for the radiological examination of 2,000 people of the town. A similar sum has been allotted for such a survey at Serampore. Within three months of commencement the Barisal centre has been able to examine only 48 cases, and in the whole period of work, which is at present fixed at one-year, only 200 cases could be examined at this rate. It is obvious that miniature radiography would have proved more advantageous at less cost, and would have given a truer picture of the condition of tuberculous infection prevailing in the locality. It is with the hope that this matter will receive due consideration in future that the present paper is concluded.

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this purpose it becomes more evident that in mass examination, clinical methods, sputum analysis, and tuberculin test cannot compete with x-ray screening in rapidity and reliability.

Recently, the experience has proved in Europe that a great many unsuspected cases have been detected by serial x-ray screening regularly conducted in military forces, police, and educational institutions.

According to a Swiss report, the average result of such mass screenings of apparently healthy young persons is the discovery of 0.5 to 1 per cent active lung tuberculosis not recognized at all, even by the affected persons themselves.

Another, a German, report gives even more detailed results:—

Out of 1,000 apparently healthy persons	Cases in need of treatment	Number with positive sputum
In the environment of T.-B.-positive cases.	100 to 150	25 to 50
In the environment of children.	1 to 2	0 to 1
In the environment of juvenile persons.	10 to 20	3 to 5
In the environment of adults.	2 to 8 to 15	1 to 4 to 8

A report from Denmark gives the following findings:—out of 1,180 students, 12 were suffering from pulmonary tuberculosis of which 7 had positive sputum.

An American report shows that mass screening gives a discovery rate of 2.9 per cent. The following table gives the more detailed account:—

TABLE

Out of 11,928 patients.	ALL PATIENTS		NEW PATIENTS						RE-EXAMINED PATIENTS					
	Total		Total		Contact		Non-contact		Total		Contact		Non-contact	
	No.	Rate %	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
	349	2.9	319	3.5	127	3.4	192	3.6	30	1.1	20	1.0	10	1.1

The latest experience in tuberculosis clinics in Europe has proved that clinical examination alone, especially in early and even sometimes in more-or-less advanced cases, is not reliable without x-ray examination.

Percussion and auscultation are of no avail in cases of early infiltration, diffuse small nodular infiltration, miliary tuberculosis, etc. In many cases of roentgenologically-visible cavities also, the classical clinical symptoms fail us. Even in patients with big cavities, auscultation signs may be absent and the negative findings of so-called

'silent cavities' is a fact well known to all specialists.

We have to admit the fact definitely that the time has gone when the doctor can rely on clinical examination only in diagnosing lung affections. Even in cases with evident dullness and catarrhal signs, the general practitioner cannot give a better diagnosis than a probable one. There are no reliable distinguishing clinical signs between tuberculous and other lung affections, e.g., bronchiectasis, bronchitis, asthma, carcinoma, pneumoconiosis, etc.

Again, examination of sputum is impracticable in mass detecting work, as it is complicated and takes up too much time and fails even in so-called 'virtually open' cases.

A merely probable diagnosis of lung tuberculosis is of little help in deciding to take preventive or curative measures.

The extent of the lesions, on the one hand, and the allergic-clinical character on the other hand, may produce so great a variety of appearances that their diagnosis depends largely on roentgenological examination, and further every step in therapeutic measures depends on the x-ray diagnosis, because various appearances require various measures.

How far a private practitioner can do his share in detecting work depends on local conditions. Whatever these conditions may be, there is no doubt that the co-operation of physicians is of extraordinary importance within the framework of anti-tuberculosis campaigns. This fact was stressed recently by Plunkett (1939). He says: 'More cases of tuberculosis are discovered by the examination of patients referred by family physicians for diagnosis than by any other generally practised method of case-finding.

It is important that no stone should be left unturned to secure the co-operation of the practising physicians in obtaining the examination of all adults, who present symptoms which might even remotely be referred to the chest'.

Detection work can be carried out on the same lines as in some countries in Europe by mass screening of select groups of the population, e.g., hospital admissions, military, police, educational institutions, state employees, and even private concerns such as mills, mines, banks, etc. It rests with the medical department to set an

example by screening once all cases admitted into the State hospitals. According to the experience of Plunkett (*loc. cit.*) this selected group reveals the greatest number of cases, viz, 1.2 per cent. 'Of special significance is the study being made of admissions to 14 general hospitals throughout New York, which not only shows the highest yield, but also shows that a surprisingly large number of cases of tuberculosis are admitted to hospitals without being recognized. No children are included, nor any persons in whom there was a previously-known tuberculosis lesion. Of the 47 new active cases already discovered, 19 had evidence in the hospital charts which might have led the attending physician to diagnose the case before discharge. However, 28 or 0.7 per cent of adult admissions were found to have active tuberculosis, although there was no evidence in the hospital records, which indicated that tuberculosis was suspected at the time of admission. If the same conditions prevailed throughout the United States, about 45,000 unrecognized cases of tuberculosis were admitted in general hospitals during 1937'.

A case with distinct clinical signs is revealed on x-ray examination generally to be in a fairly advanced condition. Unfortunately, the patient does not become aware of his disease till then, and so it is too late for any medical treatment that can stop the progress of the disease. Very few people ask for medical advice for the minor troubles which appear in the early stages of the affection; and most of the general practitioners also look upon these as minor troubles and neglect the x-ray control. It is incumbent on every medical practitioner to direct such patients to the proper centre for x-ray examination. The following points will be a guide to him under which circumstances a patient ought to be suspected of lung tuberculosis.

X-ray examination should be undertaken for,

- (1) everybody who applies for examination because suspected of or exposed to lung tuberculosis,
- (2) everybody who is under medical treatment for more than 3 months on account of any disease of the respiratory tract,
- (3) everybody who has chronic or periodic feverish conditions,
- (4) everybody who has sought for, during the last years, repeated medical advice for 'colds', bronchitis or similar diseases,
- (5) everybody who is suffering from an 'atypical' influenza, pneumonia or other diseases of the respiratory tract,
- (6) everybody who is suffering from a dry pleurisy or pleurisy with effusion (these patients should be observed for several years and be examined by x-rays at regular intervals),
- (7) everybody who spits blood,
- (8) everybody who is suffering from any extrapulmonary tuberculosis, erythema nodosum, anal fistula or abscess, cervical adenitis, diabetes or any other obstinate and obscure disease of the

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## THE DESTRUCTION OF AIR-BORNE BACTERIA

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IN a bacteriological laboratory in the media and vaccine rooms, or in rooms where tissue culture work is being carried out, the sterilization of the air is of decided advantage. The fungus infections during the monsoon in India are so common that any method ensuring even a partial success would be welcome. The old method of washing the floors and walls with an antiseptic solution has practically no value in sterilizing the air. Fumigation with formalin or other vapours has a feeble and limited action and may destroy any bacterial cultures stored in the laboratory. Pulvertaft and others (1939) have carried out an extensive series of tests by atomization of bactericidal solutions with a 'phantomyst'—an electrically operated apparatus capable of introducing the liquid antiseptic into the atmosphere in the form of a dry and penetrating mist. This mist does not condense on walls or other objects and remains suspended in the air for hours. The antiseptic in this form is in colloidal state and is generally called 'aerosol'. For its mode of action and other details the original paper of Pulvertaft and others is invaluable. Our main object in undertaking this work was to test the efficiency of the aerosols as generated by the phantomyst with a view to eliminating contamination in the vaccine-making departments at the Haffkine Institute. For preliminary work, phantomyst model A1, which is recommended by the manufacturers for rooms of 1,000 cubic feet capacity, was used but, as it was too small for the vaccine-sowing room, another spraying mechanism was substituted and found successful.

(Continued from previous column)

digestive tract, chronic otitis media of uncertain origin, and

(9) everybody who wants a certificate of health and has symptoms which may be caused by tuberculosis.

Looking at the above statistics in western countries, it is our emphatic suggestion that every centre of the anti-tuberculosis campaign should be equipped with an x-ray plant fit for serial screening and should be conducted by an experienced specialist who, by the support of public and private co-operation, would be able to carry out detection work to the utmost advantage.

### REFERENCE

Plunkett, R. E. (1939). *Amer. Rev. Tuberculosis*, Vol. XXXIX, p. 256.



### Technique

(a) *The room*.—One of the laboratory rooms (23.5 by 18.5 by 13 feet) with a cubic capacity of 5,650 cubic feet was utilized for the experiments. The room had four windows and two doors and beyond closing these in the ordinary way no special precautions were taken to make the room air-tight. The room had a ceiling fan which was kept working during all the experiments.

(b) *Bactericidal solution*.—As resorcinol has been recommended by Pulvertaft, the solution containing equal parts of glycerine and a saturated aqueous solution of resorcinol was used in most of the experiments. Chloramine T solution (aqueous 5 per cent) was also employed in some experiments.

(c) *Bacterial cultures*.—Cultures of *Bact. prodigiosum*, *Staphylococcus albus*, *Streptococcus faecalis* (enterococcus) and *Bact. coli* were used as test organisms. Watery emulsions of the growth on standard agar were standardized by Brown's opacity tubes and sprayed in the room by means of De Vilbis hand-power spray outfit (type TZ-601) consisting of a hand pump, air tank and a spray gun. This apparatus is

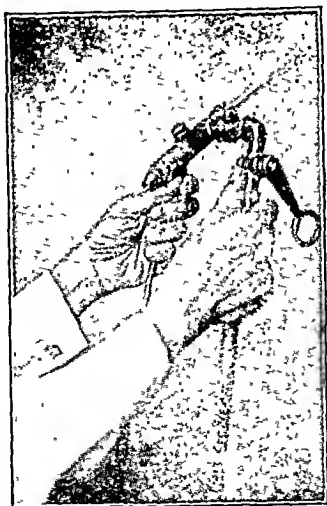


Fig. 1.—The atomizer in action.

capable of developing an air pressure of about 15 pounds per square inch and, its nozzle being adjustable, a very fine spray can be produced. In most of our experiments *Bact. prodigiosum* has been used as the test organism.

(d) *Phantomyst model A1*.—The manufacturers, Messrs. Andre (Components) Ltd., recommend this equipment for dwelling rooms, hospital wards, etc., both for insecticidal and bactericidal purposes. The disinfecting fluid emanates from the machine in the form of a cloud made up of very fine particles 'in the colloidal or aerosol state'.

(2) *Atomizer with power-driven air-compressor outfit*.—This is an assembly used for

humidifying industrial plants the details of which are as follows:—

(a) Ingersoll-Rand electrically-driven air-compressor with steel air receiver.

(b) No. 4 Amco atomizer requiring 3 c.f.m. at 30 to 35 lbs. pressure.

The atomizer consists of a tubular spraying nozzle with separate inlets for compressed air and fluid (figure 1). The air inlet is controlled by an external regulator. The fluid inlet is controlled by a built-in device which prevents atomization until the pressure of the compressed air has reached 30 to 35 pounds, and stops atomization before the air pressure has dropped below 30 pounds. These features eliminate the dripping of the fluid both at the commencement and at the end of the spraying. A very fine atomization is achieved by this sprayer though the final product is not like a cloud as in the case of the phantomyst.

### Details of experiments

1. Control suspensions of *Bact. prodigiosum* (200,000 million organisms) were uniformly sprayed by De Vilbis hand-power pump. Petri dishes containing nutrient agar were exposed for 10 minutes at three different parts of the floor of the room 30 minutes after introduction of the organisms.

A similar set of nutrient agar plates were exposed at the end of an hour. The exposed plates were incubated at 37°C. for 48 hours and colonies counted. The results are recorded in the table and are apparent from the photographs (figures 2 and 3) more than 1,000 colonies being present on each plate at the end of an hour.

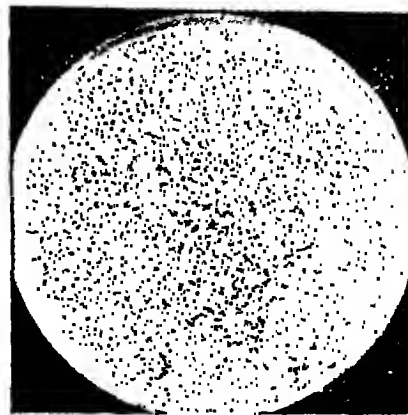


Fig. 2.—Control—Petri dish containing nutrient agar exposed for 10 minutes, 30 minutes after introduction of the organisms into the air of the room.

A similar experiment carried out without working the ceiling fan showed innumerable colonies on immediate exposure of the agar plates and about 10 colonies when exposed at the end of 15 minutes. This clearly shows that the introduced organisms had settled by gravity

in a very short time. The importance of keeping the ceiling fan working fully is apparent.

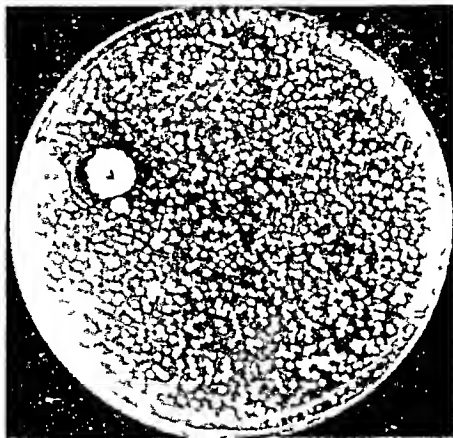


Fig. 3.—Control—Petri dish containing nutrient agar exposed for 10 minutes, 60 minutes after introduction of the organisms into the air of the room.

### Test experiments

1. *Phantomyst*.—A similar procedure was adopted for the test experiments, except that the phantomyst machine containing resorcinol solution was started immediately after dispersion of the organisms. To test the effect of the various quantities of the disinfectant the machine was run for 15, 30 and 60 minutes respectively in separate series of experiments. At the end of quarter, half, and one hour 5, 8 and 12 cubic centimetres of the solution were blown out on an average. The colonies after running the machine for a quarter of an hour (5 cubic centimetres) were numerous, while two to three colonies were always found after half and one hour running (figure 4). From these experiments, it was evident that a minimum quantity

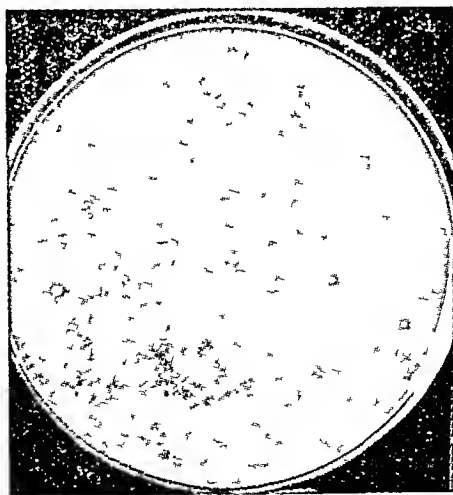


Fig. 4.—Petri dish containing nutrient agar exposed for 10 minutes, 30 minutes after disinfection by the Phantomyst (8 c.cms. of resorcinol used).

or 8 cubic centimetres of the resorcinol solution was essential to sterilize the atmosphere of the room (about 5,500 cubic feet). This almost

agrees with the result obtained by Pulvertaft in his experiments.

2. *Atomizer with power-driven air-compressor outfit*.—As mentioned previously, we had not a bigger model of the phantomyst and as the room to be sterilized was about 10,000 cubic feet we were obliged to experiment with apparatus used for humidifying the atmosphere in the cotton mills of Bombay in order to see if this would serve our purpose.

The aqueous suspensions of *Bact. prodigiosum* were dispersed in the atmosphere as in the control experiment. The resorcinol solution was nebulized by means of the special atomizer (*vide supra*). Various amounts of the disinfectant were used to find the minimum quantity and time necessary for complete sterilization. The main difference with this type of machine is that the operator has to direct the spray into all parts of the test chamber and in larger rooms would have to walk about to get equal distribution of the liquid.

The other procedures were similar to the experiments described above. It was found that 12 cubic centimetres of the resorcinol solution would give similar results to the phantomyst experiment, *i.e.*, an average of 2 or 3 colonies per plate after a quarter of an hour, as well as half an hour, instead of the innumerable colonies in the control experiment. To eliminate totally the development of any colonies whatsoever, larger quantities of the resorcinol solution were tried. It was found that 25 cubic centimetres of the disinfectant were necessary for the purpose (figure 5). Having established these facts, we substituted other organisms for *Bact. prodigiosum*.

The results are tabulated in table I.

A few of these experiments were repeated with 50 per cent chloramine-T solution using *Bact. prodigiosum* suspensions for test and were found to give similar results both in the case of the phantomyst as well as the atomizer.

*Effect on culture media*.—Pulvertaft *et al.* (1939) have stated that the plates exposed to the aerosols at their exit from the phantomyst for periods of 10 minutes or longer and then exposed to bacteria in control rooms showed no inhibition of growth. This is a very important point in the vaccine-sowing rooms and a series of experiments were carried out specially with the atomizer.

*Phantomyst*.—In the case of the phantomyst superimposed 5 per cent rabbit-blood-agar slopes were directly held for about 10 minutes over the outlet so that the mist of resorcinol solution could be seen travelling to the unplugged tubes. These tubes, as well as unexposed ones, were incubated with an equal amount of the suspension of *Past. pestis*. After incubating at 37°C. and room temperature the number of colonies were counted and found to be about the same ( $\pm 10$  per cent error).

*Atomizer*.—A slightly different experiment was repeated in the case of the atomizer, the

TABLE I  
Atomizer experiments

Type of organisms	CONTROL		TREATED AIR		Amount of resorcinol (in c.cm.) in suspen- sion in 5,500 cubic feet of air
	Interval in mins.	Colonies	Interval in mins.	Colonies	
<i>Bact. prodigiosum</i> .. ..	30 60	Infinite 1,000	15 15	3 0	12 25
<i>Staphylococcus albus</i> .. ..	30 60	Infinite Infinite	15 15	4 0	10 25
<i>Streptococcus faecalis</i> (enterococcus)	30 60	Infinite 1,000	15 15	4 0	12 25
<i>Bact. coli</i> .. ..	30 60	Infinite 1,000	15 15	4 0	12 25

tubes being fixed in a rack and placed on the floor. The resorcinol solution (25 cubic centimetres) was blown into the room and the tubes kept unplugged for 10 minutes. In a similar experiment the media did not show any inhibitory effect as compared to the control.

**Practical application.**—This method of sterilizing the air was introduced into the plague vaccine-sowing room and the antirabic department. Though this method has been in practice for about a month only, the results are very encouraging as is apparent from the following figures.

As after monsoon the contamination goes down normally, the figures for the period corresponding to the time of disinfection by atomization for the previous two years are quoted below :—

	Total number of flasks sown	Contamination, per cent
After the introduction of atomization—		
29th September to 19th November, 1939.	1,086	2.0
Previous to atomization—		
During 1937 (same period)	1,133	5.0
During 1938 (same period)	1,128	4.4

#### Summary and conclusion

1. As claimed by Pulvertaft *et al.* (1939) the resorcinol solution nebulized by the phantomyst is an efficient method for air sterilization of rooms.

2. An alternative method by using a special atomizer worked by compressed air has been found to be equally effective if larger quantities of the bactericidal fluid are used.

3. Since our experience with atomization is limited, we cannot say whether this method is

universally applicable but we can recommend it for laboratories. If compressed air is available the other outfit (excluding the power unit) costs about Rs. 100.

We wish to record our thanks to the Anglo-Siam Corporation and Messrs. Ingersoll-Rand (India) Ltd. of Bombay for the loan of the machines.

#### REFERENCE

Pulvertaft, R. J. V., *et al.* (1939). *Lancet*, *i*, p. 443.

#### A STUDY ON THE TOXICITY OF THE BILE ACIDS AND THEIR DERIVATIVES PREPARED FROM INDIAN OX BILE

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PILLS or capsules containing the extract of ox bile are often prescribed for stimulating the action of the liver and for favouring the absorption of fat by the intestine. In this respect natural bile salts, being of more constant composition, are often preferred. But, while preparing such salt from the bile collected from the local slaughter-house, it was noticed that the Indian ox bile is invariably poor in its bile-salt content. Again, as the bile acids and their derivatives possess a strong depressant action on the heart and at the same time are markedly hæmolytic, any work on the preparation of such compounds, particularly from a bile of the above nature, warrants a study of the toxicity of the products that are to be prepared from it. Accordingly, the general characteristics of the Indian ox bile collected over a period of six months from March to August were first noticed, and then the pharmacological properties of the salts, as well as of certain products (sodium cholate and sodium dehydrocholate) derived

from them, were studied. All these observations are embodied in this paper.

### Experimental

Usually the gall bladders were secured from the local slaughter-house and kept in an ice-cold temperature till they were handled for extracting the bile present. The total bile was extracted from each of them and analysed for noting the characteristics as shown in table I. The biles were of a yellowish-green colour and alkaline in reaction. The pH from a direct-reading glass-electrode pH meter (Leeds and Northrup), the specific gravity by the bottle method, the refractive index by Abbe refractometer, the surface tension by the drop method, and the viscosity were noted in each sample at 35°C. The percentages of total solids as well as the ash on incineration were also determined. Table I gives the average maximum and minimum figures from an analysis of 600 samples.

alcohol. The alcoholic solution, on dilution with ether, afforded the bile salt in granular form. These sodium salts were further purified in the way described in the process of purification of sodium cholate, and subsequently dissolved in water to the required concentration.

*Hæmolysing property.*—All experiments in which substances were tested for hæmolytic action were carried out in the following manner. The red blood cells were obtained from the blood of a normal sheep. The plasma was removed by centrifuging and the cells then washed five times with 0.9 per cent sodium chloride solution. A 2 per cent suspension was made of the washed cells in normal saline. A tube containing 1 cubic centimetre of this suspension, mixed with 1 cubic centimetre of 0.9 per cent saline, served as a control and the various other tubes contained 1 cubic centimetre of the suspension, the amount of test solution, as shown in the table II, and the volume of water or saline required to make the

TABLE I

### Characteristics of Indian ox bile

	pH	Density	Refractive index	Surface tension in per cent of water	Viscosity	Total solids	Ash, per cent
Maximum ..	7.35	1.0210	1.3456	61.80	1.487	8.0	1.0
Minimum ..	6.9	1.0140	1.3410	62.5	1.20	5.2	0.7
Average ..	7.15	1.0178	1.3438	62.46	1.362	6.7	0.9

The total amount of the bile collected in a day was refluxed with sodium hydroxide (8 gms. per 100 c.cm. of the bile) for several hours and the cholic acid formed was isolated by acidifying the resulting solution. The acid thus obtained on purification and crystallization from ethyl alcohol melted at 196° to 197°. The yield on the average was 15 to 18 gms. per litre of the bile. The crystallized cholic acid exhibited all the properties characteristic of the compound. The acid was dissolved in a small amount of alcohol and treated with a solution containing the molecular amount of sodium carbonate. The sodium salt of the cholic acid was then precipitated out by the addition of ether. It was redissolved in dilute alcohol and again precipitated out with ether. The purified sodium salt thus obtained, was dissolved in water to afford the solution required for the pharmacological investigations (*vide infra*). The cholic acid was oxidised by a chromic acid mixture in glacial acetic acid and the dehydrocholic acid found was collected, washed well with water, and crystallized from ethyl alcohol. It melted at 233° to 235°C., gave no Pettenkofer's reaction and was readily soluble in sodium carbonate to afford a pale yellow solution.

The natural bile salt was prepared by evaporating the raw bile with animal charcoal and subsequent extraction of the pasty mass with

total volume 2 cubic centimetres in each case. After being shaken to ensure complete mixing, the tubes were allowed to stand at room temperature (31°C.). Hæmolysis determinations were made at intervals by centrifuging and by evaluating the intensity of red colour in the supernatant liquid and also the amount of red blood cells left behind in certain cases. The supernatant solution of the control tube was found to remain colourless even after 24 hours at the room temperature.

*Tests for intravenous toxicity.*—For studying the toxicity of the above three salts—the natural bile salt (2 per cent solution), sodium cholate (2 per cent) and 'dehydrocholin' (5 per cent), male white mice from our own stock and of average weight 20 to 21 grammes were taken and the solutions were injected intravenously. Table III shows the survival rate of the animals so treated.

Sodium dehydrocholate has been described as practically non-toxic (*cf.*, Neubauer, 1923) and at the same time exerts a definite choleric (Wakefield *et al.*, 1929) as well as a powerful cholagogic action (Sterner *et al.*, 1931). It was accordingly considered to be of interest to see whether it further exerts any influence on the toxicity of other bile acid salts. Recently, sodium dehydrocholate has been found to exert a favourable influence in increasing the tolerance

to arsenic therapy (*cf.*, Jacchia and Truffi, 1934; Robba, 1937). Each of a set of mice was injected intravenously with 8 mgm. of sodium dehydrocholate (dehydrocholin 5 per cent) and after eight days they were divided into two

### Discussion

From table I it is evident that the average total solids in gall-bladder bile is 6.7 per cent and the density 1.0178; but the above two data as recorded in Smith's *Manual of Veterinary*

TABLE II  
*The hamolytic effect of different bile salt solution*

Substance	Cubic centimetres of sheep cell suspension (2 per cent)	Test solution in c.cm.	Distilled water in c.cm.	Normal saline in c.cm.	Final concentration of the salt, per cent	HÆMOLYSIS	
						After 2 hours	After 24 hours
Sodium dehydrocholate 2 per cent sol.*	1	1.0	..	..	10.0	—	—
	1	0.5	0.5	..	5.0	—	—
	1	0.25	0.75	..	2.5	—	—
Sodium cholate 4 per cent sol.	1	1.0	..	..	2.0	p	p
	1	0.5	0.5	..	1.0	p	+
	1	0.25	0.75	..	0.5	+	+
	1	0.25	..	0.75	0.5	—	—
Bile salt 4 per cent sol.	1	1.0	..	..	2.0	+	+
	1	0.5	0.5	..	1.0	+	+
	1	0.5	..	0.5	1.0	+	+
	1	0.25	..	0.75	0.5	p	p

\*In all the experiments the sodium dehydrocholate solution used was the 'dehydrocholin' of Bengāl Immunity Co., Ltd., Calcutta.

+ Complete hæmolysis.

p Partial

— No

groups. One group was injected with different doses of natural bile-salt solution (2 per cent) and the other with those of sodium cholate (2 per cent). A fresh batch of mice treated with the minimum lethal dose of the bile salt served

*Physiology* (1921) are 9.6 and 1.022 to 1.025, respectively. The alkalinity (pH = 7.15) of the Indian ox bile is also not so pronounced. The bile salt isolated from the bile, however, is extremely hæmolytic as usual and seems to exert

TABLE III  
*Intravenous toxicity of different bile salts on mice : average weight 20 to 21 grammes*

Substance	Dose in mgm.	Number of mice	Number of mice dying in a day				Survival
			1	2	3	4	
Bile salt .. ..	2	3	..	..	..	..	3
	3	3	..	..	..	..	3
	4	6	6	..	..	..	..
Sodium cholate .. ..	2	3	..	..	..	..	3
	3	3	..	..	..	..	3
	4	4	..	1	1	..	2
	5	6	6	..	..	..	..
Dehydrocholin .. ..	4	3	..	..	..	..	3
	8	6	..	..	..	..	6
	16	6	..	..	..	..	6
	20	6	..	..	..	..	6
	24	6	..	..	..	..	6
	30	8	5	3	..	..	..

as control in the former case, and another treated with the minimum lethal dose of sodium cholate served as control in the latter case. Table IV shows the result of this investigation.

a direct action on the red blood cells. Even a 0.5 per cent solution of the salt in 0.8 per cent saline was found to be hæmolytic, whereas the contents of a similar tube containing the cells suspended in 0.8 per cent saline showed no sign

of hæmolysis. On injecting the minimum lethal dose into mice symptoms of immediate depression and blackening of the skin were invariably noticed. That Indian ox bile is of poor quality was also evident from the amount of cholic acid isolated by hydrolysis of the bile.

to 50 per cent. The significance of this observation seems to be that, in clinical applications of the natural bile salts, the tolerance of the medicament may be considerably increased by previous treatment with sodium dehydrocholate which is again a good bile stimulant (Stern

TABLE IV

*Influence of sodium dehydrocholate on the toxicity of other bile salts in mice (average weight 20 gm.)*

Drug	Dose in mgm.	Sodium dehydrocholate, mgm.	Number of mice	Number of mice dying in a day				Survival
				1	2	3	4	
Bile salt .. ..	4	..	3	3	..	..	..	..
	4	8	12	..	..	..	..	12
	6	8	12	2	2	..	..	8
	8	8	12	3	2	1	..	6
Sodium cholate ..	5	..	3	3	..	..	..	..
	6	8	6	1	..	..	..	5

The yield never exceeded 18 grammes per litre, whereas Wieland and Weyland (1920) recorded a yield of 25 grammes of cholic acid per litre of the bile. The sodium cholate is also considerably hæmolytic (*vide* table II), but is slightly less toxic than the natural bile salt. This salt also on injection produces cardiac depression with subsequent collapse and death.

The sodium salt of dehydrocholic acid, obtained by oxidizing the cholic acid is, however, found to be practically non-hæmolytic (*cf.* Ziegler, 1931 and 1932). It is also considerably less toxic than the other salts. Table III shows that for male white mice the minimum lethal dose in milligramme per gramme body weight is 0.2, 0.25 and 1.5, respectively, for natural bile salt, sodium cholate and sodium dehydrocholate. During the course of injection of these various salts it has been invariably noticed that the bile salt, as well as the sodium cholate, produces tissue necrosis (*cf.* Ziegler, 1930). The sodium dehydrocholate is, however, free from such side reaction. On injecting the latter salt in a dose of 0.8 mgm. per gramme, or higher, into mice, a peculiar symptom of dancing round the cage was noticed. The animals began to run to and fro, then suddenly quieted down and started gasping. This salt is, however, better tolerated by the mice if it be injected at a lower concentration or after dilution with normal saline. Sodium dehydrocholate is further found to lower the side reactions and the toxicity produced by the administration of natural bile salts. Thus, from table IV, it is evident that the mice treated with 8 mgm. of sodium dehydrocholate tolerated the minimum lethal dose (0.2 mgm. per gramme) of the natural bile salt, and the mortality in the group of animals treated with a dose of 0.4 mgm. per gramme fell

*et al.*, 1931) without any appreciable toxic property in its clinical doses (*cf.*, Adlersburg and Neubauer, 1926; and Wakefield *et al.*, 1929).

### Conclusion

The Indian ox bile collected from the local slaughter-house is invariably of poor quality.

The bile salts present in it are toxic and extremely hæmolytic as usual, but the sodium salt of dehydrocholic acid, prepared by oxidising the cholic acid isolated from the above bile, is much less toxic and is practically non-hæmolytic.

From the preliminary experiments so far carried out, it seems that sodium dehydrocholate increases the tolerance and lowers the side effect produced after the ingestion of natural bile salts.

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## ROLE OF CALCID FUMIGATION AS A RATICIDAL AND PULICIDAL MEASURE IN ANTI-PLAGUE CAMPAIGN

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BUBONIC plague is primarily and essentially a disease of rodents, especially rats, and is carried from rat to rat by fleas. It may however under suitable conditions affect man through the agency of fleas. Man's contact with the infection depends upon his contact with the rat and its fleas. Man's chance of escape from this disease is therefore conditioned upon the effectiveness of the campaign against these pests.

Were it possible to exterminate all rats within the endemic areas or render them immune, plague would disappear immediately. The possibility of the total extermination of rats has exercised the brains of people of all lands and ages, but the problem has yet to be solved. The animals breed at such a rate as to render futile all attempts at extermination. Calculation of the reproductive powers of rats bewilder imagination—one pair may give rise to as many as 900 rats in one year.

Fortunately, it is found by experience that the total elimination of rats in a locality is not absolutely essential for the eradication of plague. If the rat population is kept within low limits, rat centres are destroyed and such rats as do exist are well scattered and not congested, rat plague will disappear from a locality.

Under the present circumstances, therefore, the mainstay of all anti-plague measures, besides the permanent works including rat proofing, sanitary measures and health education of the masses, is rat and flea destruction so as to reduce their population to a low figure. This is a great safeguard against rapid spread of plague.

The special plague department, Hyderabad Deccan, carries on a continuous and well-organized anti-rat campaign throughout the year with very successful results. The anti-rat campaign as carried out by this department consists of baiting, trapping and fumigation.

### *Advantages of fumigation over baiting and trapping*

(1) Traps and barium carbonate baits are only partially effective as they do not destroy the fleas at all. Since fumigation deals with both rats and fleas, it is undoubtedly the best of all available temporary plague measures. One of the most difficult problems in plague prevention was how to deal adequately with both rat- and flea-infested houses. The situation is aptly summed up in the 1932-35 report of the Haffkine Institute, Bombay, which says:—

'In the past, rat baiting and trapping combined with the use of kerosene oil emulsion have been our chief methods of attack. These methods do not prove effective; the results obtained were hardly commensurate with the amount of labour involved. But the position has entirely changed with the advance of industrial chemistry which has placed at our disposal a number of calcium cyanide preparations which when suitably used ensure a rapid and effective destruction of rodents and, what is very important, their fleas. Baiting and trapping of rats did not affect the flea problem at all'.

(2) Recent observations have shown that favourable incubating conditions (temperature and saturation deficiency) prevail in underground rat holes and that infected rat-fleas can easily survive the usual short off-season during the summer months, and are probably therefore a factor in the carrying over of plague from one season to another.

If that is true, fumigation will prove to be the most valuable measure known for the destruction of these incubating fleas and in preventing the recrudescence of plague.

(3) Fumigation is the quickest and surest method of rat destruction.

The wily rat is taken unawares and nothing is left to its choice. None of the rats and fleas in the rat holes are left alive.

(4) As most of the rats after fumigation die in the burrows out of sight, the process is less annoying to certain sections of the public who object to seeing rats being trapped and killed. The bad smell from decomposition of baited rats due to death in inaccessible situations is also avoided. It is a very important factor in actual practice.

(5) Fumigation kills not only rats and fleas but also snakes, ants, porcupines, and termites, and therefore ready co-operation of the public is usually forthcoming.

(6) Fumigation is easily applied—all that is required is to blow a very small quantity of the material into a rat hole, to close it and leave it—no rats or fleas will remain alive in it.

(7) The fumigation method is simple and requires less staff. Expenses required for repairs are also negligible.

(8) Under proper supervision and in trained hands, fumigation can be done with hardly any danger at all to human beings.

(9) Because of the advantages mentioned above fumigation is gradually replacing other measures such as baiting and trapping.

Baiting may however be used as an adjunct to fumigation, and trapping is essential to find the index of the prevalence of rats in any area (rat-density), as an indicator of the results of baiting, for catching rats that are bait-shy and have escaped baiting, and as a means of obtaining flea-indices and making flea surveys. Baiting and trapping will also be required to destroy rats which cannot be dealt with by fumigation, such as those residing in inaccessible situations,

and in thatched and tiled roofs which unfortunately abound everywhere.

### Fumigation

The use of poisonous gases for the destruction of rats has long been recognized and adopted by sanitary authorities all over the world.

Various substances have been used for this purpose, but only three need be seriously considered as fumigants, namely, carbon monoxide, sulphur dioxide, and hydrogen cyanide.

#### 1. Carbon monoxide

This gas is produced by the incomplete combustion of coke or charcoal in a closed stove. It is usually combined with carbon dioxide when used as a fumigant. Its dangerous nature and the complicated machinery required for its production preclude its usefulness on land, though it is still employed for ship deratization under proper supervision. It is reputed to be non-lethal to fleas.

#### 2. Sulphur dioxide gas

Sulphur dioxide gas can be generated from Clayton machines. In the Punjab a convenient method of smoking rat holes with sulphur dioxide has been in use in the form of candles called *bhoosa battis*, which are a modification of Lane's *neem battis*. This consists of a mixture of chopped straw, red pepper, sulphur, potassium chlorate, and potassium nitrate wrapped in an oily paper and provided with a gauze wick which is lit and placed in the burrow.

Sulphur dioxide gas is relatively cheap, easy to generate and less dangerous to handle, but apart from this, it cannot compare with hydrogen cyanide gas in efficiency, speed of action and ease in handling. It also corrodes or tarnishes metals, paints, etc., and ruins food-stuffs and cereals, fabrics and delicate articles; it is also less diffusible and has lower penetrating powers. After experiments here in the laboratory and carefully controlled trials in the field, it was proved that cyanogas was much more efficacious than sulphur dioxide. Use of sulphur dioxide was given up by this department about five years ago.

#### 3. Hydrogen cyanide

Fumigation with hydrogen cyanide has been employed for a number of years particularly for the destruction of vermin, and pests in ships, and for the destruction of bugs in infested houses. In fruit-farming too, certain destructive pests have been successfully attacked by this means. But it is only in recent years that experiments have been carried out which have proved that cyanide products are powerful lethal agents for rats and rat-fleas and that they are therefore valuable weapons in the fight against plague.

There is no question of the superiority of cyanide products over carbon monoxide or sulphur dioxide gas. Both experiments and practical experience here have proved time and again

their deadly effect on rats and fleas, their diffusibility, penetrating power, toxicity in small doses, and harmlessness to delicate articles.

Many products have been used.

(a) Pure hydrocyanic acid is used in some countries for fumigation of vessels under proper supervision, but it is too dangerous to use on land.

(b) Zyklon-B consists of 95 per cent hydrocyanic acid and 5 per cent chloropicrin (as a warning gas) impregnated in Fuller's earth or kieselguhr. It is used for fumigation of ships under supervision but is too dangerous for use on land.

(c) Calcium cyanide products:—

For practical purposes, only two preparations, viz, calcid and cyanogas dust 'A', are worth considering as far as fumigation on land is concerned.

(i) Calcid is supplied in briquettes (tablets) of 20 grammes each. These are composed of calcium cyanide 88.5 per cent and 11.5 per cent of almost pure lime. Powdered calcid produces just over 50 per cent of available hydrocyanic acid.

(ii) Cyanogas 'A' dust is a compound consisting of 45 per cent calcium cyanide and 55 per cent slaked lime. Cyanogas produces about 23 per cent of available hydrocyanic acid. Cyanogas is supplied in the form of powder and a special foot pump is provided for use.

Both calcid and cyanogas 'A' owe their value to the fact that when powdered and exposed to air these are acted upon by the atmospheric moisture, form hydrocyanic acid gas, and leave behind a residue of slaked lime.

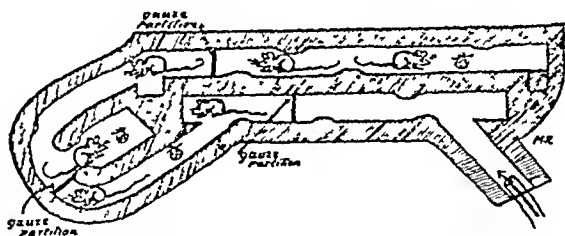


Fig. 1.—Artificial rat-burrow for experimental purposes.

#### Experimental data

Experiments were carried out at the plague department laboratory, Hyderabad Deccan, to measure the relative potency of 'cyanogas and calcid for fumigation purposes.

An artificial run (figure 1) 5 inches deep, 5 inches wide and 18½ feet long consisting of four divisions of equal length separated by fine wire gauze is constructed. This is roofed in by glass held down at the sides with mud, so that the whole run is open to observation. The same run is used throughout.

#### Method of testing

For each test 2 adult rats and a muslin bag containing 5 fleas are introduced into each section of the run except in the first. Thus 6 rats and 15 fleas are used for each test. To the

open end of the run the nozzle of the 'baby duster' or cyanogas pump is inserted and packed round with mud.

A measured quantity of the product to be tested is blown into the run and a stop watch started. As soon as the powder escapes from the opening at the other end, this is sealed with mud. The rats are watched through the glass, and, as soon as they appear to be dead, the time is noted and the glass roof removed to expose the rats to fresh air. The rats are left in the open channel for another 10 minutes and then put in cages and removed to a room for examination after 24 hours. The time of exposure given in the tables is the time between the blowing in of the dust and the removal of the glass roof. The number of escapes are the animals that are found alive on the second day in cages. The muslin bags are removed from the run at the same time as the rats, and fleas are kept in glass jars covered with muslin and examined the next day.

#### A. Cyanogas 'A' dust

Number of experiment	Quantity of product used, grammes	Duration of exposure before breathing stopped, minutes	Deaths, rats	Deaths, fleas
1	5	..	..	..
2	10	..	..	..
3	15	..	..	..
4	20	5	1	5
5	30	2	2	5
6	40	2	2	15
7	50	10	4	15
8	60	10	6	15

#### B. Calcid briquettes

1	1	..	..	5
2	2	5	1	10
3	3	8	3	10
4	4	8	4	10
5	5	7	5	15
6	6	7	6	15

Note.—Six rats and 15 fleas are used during each experiment and the findings confirmed by several repetitions.

#### Relative potency of the two products tested

These results are considered to demonstrate that 6 grammes of calcid are at least as efficacious as 60 grammes of cyanogas dust and are sufficient to kill all rats and fleas in an ordinary rat-run.

The hydrocyanic acid content of calcid being only twice that of cyanogas, it appears that the greater efficiency is in part due to the form of blower recommended for use with calcid. This blower grinds the blocks of calcid into a very fine powder and blows it with sufficient force to distribute the powder in lethal quantity to the extreme end of an eighteen-foot run.

The cost of cyanogas powder is Re. 1-8-0 per lb. and of calcid Rs. 3-4-0 per kg. (2½ lb.). As efficient results are obtained with one-tenth the quantity of calcid this product is far less expensive for fumigation of rat runs. These poisonous chemicals should only be used by trained and trustworthy workers, and greatest care is necessary to see that by no possibility are people or domestic animals exposed to the fumes, and no rat-run should be fumigated until all terminal and lateral openings are ascertained and closed.

#### Calcid and cyanogas compared as fumigants

1. Laboratory experiments described above and regular and extensive field-work carried out in the inhabited areas in this State have proved that calcid is much more efficient and economical than cyanogas.

2. In spite of its high potency as a rat and flea destructor its use is quite safe in trained hands. This has been definitely shown by practical experience spread over several years. Furthermore, it is not necessary to vacate the houses for any length of time. The occupants can return very soon after the operation is finished.

3. Furthermore, the effects of calcid are more lasting and the rat holes once fumigated with calcid are not re-opened for a much longer period than when closed after cyanogas.

4. Calcid too is supplied in solid briquettes which do not evolve any great amount of gas when merely exposed to the air unpowdered. It is far easier to measure and regulate the quantity and thus avoid unnecessary waste of materials and time, than is the case with cyanogas 'A' powder.

5. A special apparatus ('baby duster') is provided by the makers for using this preparation. It is a combined grinder and blower. It grinds the tablets to a very fine powder and at the same time a powerful fan drives the powder further along the burrow and does it more quickly and more evenly than is the case with the cyanogas pump.

In the case of cyanogas 'A' dust the blower is not so efficient and deposits a considerable part of the powder in that part of the burrow nearest to the blower, only a small proportion being carried into the deeper recesses.

6. The blower is worked by hand and is much lighter and easier to work than the cyanogas foot-pump. Considering the labour involved and the range of efficiency, calcid is much superior to cyanogas and should be recognized as the fumigant of choice for rat and flea destruction.

#### Calcid fumigation

The plague department, Hyderabad Deccan, gave up the use of cyanogas 'A' dust four years ago and have adopted calcid fumigation as a rat- and flea-kill measure with successful results. The rat-density and flea-index

have gradually come down, chiefly as a result of intensive and organized calcid fumigation carried out continuously throughout the year. The reduction in the flea-index is very marked and significant; while it rose to as high a figure as 13 in 1934, it did not go beyond 5 in 1937. Figure 2 shows the flea-index and rat-density week by week for the year 1934, before calcid fumigation was started, and for the year 1937, two years after the adoption of calcid fumigation. These low figures are partly responsible for the low incidence of plague in Hyderabad City (Deccan) during the last three years.

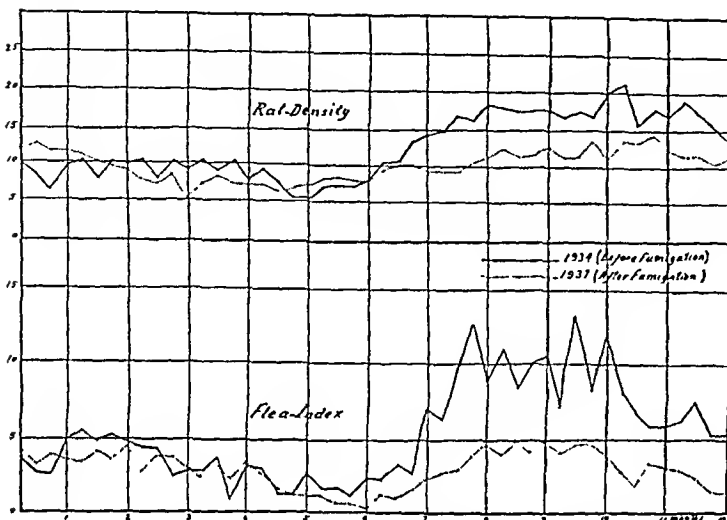


Fig. 2.—Comparative chart showing rat-density and flea-index before and after calcid fumigation.

The number of houses fumigated and number of rat holes closed annually in Hyderabad city and suburbs are given below :—

Year	Houses fumigated	Rat holes closed
1936 ..	67,603	866,321
1937 ..	83,841	1,158,721
1938 ..	66,357	881,974

Hyderabad Deccan appears to be one of the few cities in India where calcid fumigation has been carried out on an extensive scale.

It is interesting to note that all this has been done without an untoward accident of any kind.

On account of the dangerous nature of the preparation, calcid has not yet been taken up for use on an extensive scale in many parts of India. With proper control and under trained supervision there is no danger of any kind in operating this valuable product in inhabited areas, as has been done so successfully in Hyderabad city. These operations have now been started throughout the Hyderabad Dominions with excellent results.

Fumigation is carried out under the supervision of a trained medical officer, health inspector, or health sub-inspector, and all necessary precautions are undertaken. An antidote outfit is always kept at hand in case of emergency.

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## PROVISION OF LATRINE ACCOMMODATION IN VILLAGES

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BORE-HOLE latrines work satisfactorily and there is no nuisance on the ground of smell. Further, they require very little space for erection. A bore-hole latrine used by four persons will last almost permanently without the necessity of its being shifted from one place to another, provided tree growth is encouraged around it. If there are more than four persons in a family it is recommended that one seat be provided for every four persons. The tree or crop may be lime, orange, mango, sapota, country goa, papaya, banana, margosa, pungan, raintree, pocarasu, avisichettu, or seema-chintachettu or any other tree which may suit the convenience of the parties concerned. One individual on a mixed diet evacuates 6 oz. of night-soil and 40 to 50 oz. of urine per day and the nitrogen content of these comes to about 10 pounds of organic nitrogen in one year. The idea of growing trees is to deplete the soil of this and thus keep it sweet and clean round the latrine. Trees near bore-hole latrines grow very much better than trees elsewhere under similar conditions. The writer had occasion to put a latrine between two trees on a road margin. The two trees on either side of the latrine swelled in girth and the leaf growth increased enormously within a month, in marked contrast to the other trees that were in the same row and did not show any extra increase in size. It was a useful demonstration to the public of the high manurial value of a bore-hole latrine. From the public health point of view it keeps the soil and the air pure. Further, the nitrogen can be utilized for the growth of useful fruits rich in vitamin C, or of green leaf for cattle or goats, or converted into edible green leaves rich in vitamin A. If preferred, the leafy growth of trees can be cut and used as green manure. This is greatly in demand especially in deltaic areas. Tree growth will keep the place cool, allay the dust nuisance, and will add to the fuel and thus release cowdung for the fields; as it is now, a certain amount of dung is converted into dung cakes for fuel, which is an economic loss.

(Continued from previous column)

For each machine three men are necessary, supplied with calcid, the pump, a spade and a basket of damp clay or mud for sealing rat holes.

It is not intended to discuss in this article the details of the actual operation of calcid fumigation and the precautions to be taken.

My thanks are due to Dr. H. Hyder Ali Khan, F.R.C.S. (Edin.), the Director, Medical and Public Health Department, H. E. H. the Nizam's Government, for his permission to publish these notes.

In these days when much attention is paid to the conservation of humus in soil of intensively cultivated areas, every attempt should be made to conserve humus, especially when lack of attention in dealing with the night-soil problem is a distinct danger to the community. With a little amount of forethought this dangerous material can be converted into valuable humus. Calculating organic nitrogen value on the basis of groundnut cake cost at Rs. 50 per ton which contains 8 per cent nitrogen, the manurial value of the contents of a bore-hole used by four persons will be worth about Rs. 12-8-0 in a year. The capital cost per individual for providing a bore-hole latrine comes to Rs. 25 for one seat Rs. 6-4-0 per individual 4 users, and this initial outlay, in addition to solving the latrine problem gives an indirect return of 50 per cent which will more than cover the interest, depreciation and maintenance charges. The indirect benefits to the garden by letting in the air to a depth of 18 feet in soil are (1) aeration of deeper layers of soil, (2) by giving facilities to tree roots to go down near the sides of bore holes potassium from the deeper layers of soil will be sucked up to the surface, (3) increase in the live and active layers of the soil. Thus the bore-hole latrine scheme can be made to pay for itself and valuable organic matter can be conserved in the soil, and human beings will get the benefit of suitable latrine accommodation resulting in diminution in the incidence of hookworm and other intestinal parasites, and cholera, typhoid, diarrhoea and dysentery bacilli will be killed by coming in contact with septic material. The rich and certain harvest in the betterment in the public health is a benefit of incalculable value. A rough estimate is given below :—

		Rs.	As.	P.
Latrine slab	..	2	8	0
Boring charges	..	1	8	0
Zinc sheet	..	10	0	0
Timber, etc.	..	3	0	0
Construction charges	..	3	0	0
Unforeseen charges	..	5	0	0
<b>TOTAL</b>	..	<b>25</b>	<b>0</b>	<b>0</b>

For places where other materials such as tatties, bamboo matting, coconut or palmyrah leaves, or date matting are available, or where planks are cheap, the cost of zinc sheets can be avoided. The main thing is to have the bore-holes and slabs, and to adopt any suitable screen from old zinc sheets, empty tar barrels or oil barrels. Mud walls can be erected wherever possible.

The writer of this note has observed bore-hole latrines used by four persons per seat working for more than three years without a tendency to fill, without emitting smell and without the necessity of reboring. The Director of Public Health, Madras, inspected some of the latrines in the Nilgiris and had occasion to remark on the

(Continued at foot of next column)

## NOTE ON THE PRODUCTION OF AGGLUTININS IN THE BLOOD OF INDIVIDUALS AFTER PERORAL AND SUBCUTANEOUS VACCINATION BY TYPHOID AND PARATYPHOID VACCINES

By E. SOMASEKHAR, M.R.C.S., L.R.C.P., D.P.H.,  
F.R.C.S. (Ed.)

THERE have been numerous reports by various workers on the production of agglutinins in the blood after the administration of vaccines by mouth. The following investigations were undertaken to study the production of agglutinins in the blood of volunteers, using such vaccines as were available locally and have been used in the prophylaxis of enteric fever.

The subjects, 94 in number, were workmen in the medical, loco. and engineering departments

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absence of smell and inquired whether any special arrangements had been made to eliminate it. All the sanitary staff in the district are impressed with the advantages, or real necessity of having tree growth, and the secret of success was in their understanding the details and implicitly carrying them out as a routine.

### Summary

1. An economic method of approaching the problem, the scheme being self supporting, is outlined.
2. Tree planting is encouraged with direct and indirect benefits. One cannot over-emphasize the necessity for tree planting.
3. Soil is kept sweet and pure.
4. Destruction of bacteria of typhoid, cholera and dysentery from carriers from the moment of evacuation occurs, as they come in contact with septic material.
5. Hookworms and other intestinal worm infections will be prevented from spreading, as contact with feet of human beings is avoided and flies cannot get access to the disposal chamber.
6. Green leaf and manure is made available and more profitable, and vitamin-yielding fruits as well as leafy matter can be made available.
7. It is æsthetic and entirely free from bad odours or gases.
8. It is the most natural method of dealing with the problem. Dangerous filth of human beings used as food for plants and plant products (only too welcome to human beings) are made readily available.
9. Contamination of wells rarely happens in practice and can be completely eliminated if for 35 feet round latrine seats trees are grown at intervals of 6 feet.



of the M. and S. M. Railway at Guntakal. A preliminary examination of their sera revealed that agglutinins were not present in their blood, except in four who showed a titre varying from 25 to 50 for *Bacillus typhosus*. These were reported to have either had inoculations or attacks of enteric fever previously. These four and one absentee were excluded and the remaining 89 volunteers were divided into four groups. The first three groups consisted of 29, 29 and 27 individuals, respectively, while the fourth constituted a special group of only four volunteers.

The men in each of the three major groups were workmen doing heavy manual labour and were living in the railway colony, or just outside it, obtaining their food supplies from the same area and water from the same source. The average ages of each of these groups were 29.31, 32.5, and 27.11 years, respectively. Their habits of living were similar in nature and the incidence of previous infection, if any, was insignificant. This was borne out by the absence of specific agglutinins to either *B. typhosus*, or the paratyphoids prior to their coming under observation.

None of them developed any illness, of any serious nature, during the 12 months they were under observation, so that the question of any non-specific response which would influence their agglutinin titre at the end of the year was also eliminated.

It should therefore be noted that these groups were more-or-less homogeneous as regards their age, work, diet, and the incidence of previous and subsequent infection if any.

To each individual of these groups was administered vaccine either by mouth or subcutaneously as noted below :—

*Group I. Oral vaccine, bilivaccine (La Biotherapie Laboratory, Paris)*

Received adult dose consisting of three tablets of bile pills followed by three tablets of vaccine during three successive days. The bile pill was swallowed in the morning on an empty stomach, and this was followed by vaccine tablet  $\frac{1}{4}$  hour later. No food or drink was allowed for at least one hour after. This was repeated on the following two mornings.

*Group II. Oral vaccine, typhoral (Bayer)*

Received adult dose of one dragée (tablet) of typhoral (Bayer) in the early morning on an empty stomach; this was repeated the following two mornings and no food or drink was allowed for an hour after.

No preliminary administration of bile.

*Group III. Subcutaneous inoculation, trivalent TAB vaccine (Guindy)*

Injected subcutaneously with 0.5 c.cm. trivalent (TAB) vaccine followed a week later by 1 c.cm.

*Group IV*

Received three tablets of vaccine (bilivaccine, La Biotherapie Laboratory, Paris) per day on three consecutive mornings after a preliminary bile pill.

Composition of vaccine administered was as follows :—

*Bilivaccine (La Biotherapie Laboratory, Paris)*

Each tablet contains of 50 mgm. of heat-killed and desiccated Eberth bacilli and para 'A' and 'B' of different origins.

*Typhoral (Bayer)*

A proprietary product containing the antigens effective against typhoid, and paratyphoid A and B in lysated form.

*Prophylactic trivalent vaccine (King's Institute, Guindy)*

Each c.cm. contains :—

*B. typhosus* 1,000 millions.

*B. para 'A'* 750 millions.

*B. para 'B'* 750 millions.

*Method of examination of blood*

From individuals in groups one and three, 5 c.cm. of blood were drawn and sera tested at intervals of one to two weeks, until the ninth week and thereafter during the ninth month, and also at the end of one year. In group two the sera were tested at the end of one week, nine months and 12 months.

The technique for agglutination was by the macroscopic method, since it was the routine in use and it was considered more accurate, and a large number could be tested at a time. The dilutions used ranged from 25 to 3,200 in cases of *B. typhosus* until the ninth week, thereafter to 800, while those for A and B ranged up to 200 during the whole period of observation. Altogether 416 sera were examined.

The composition of the suspension used for the agglutinin test was 0.1 per cent formalinized emulsion of *B. typhosus* para A and para B, containing 1,000 millions of organisms per 1 c.cm. standardized by the opacity method, and the test-tubes in which the test was made were incubated in a water bath at 55°C. for two hours. The racks were allowed to cool and careful readings taken against a saline control at each examination.

The agglutinins tested were for general response and not for either H or O, separately. The results and the reactions are tabulated in table I which are self-explanatory.

In tables II and IIA are given the results of the tests in the groups treated orally with preliminary bile and vaccine pills—ordinary dose—and three times the advocated dose. It will be seen that no agglutinins were present in the



number tested with ordinary dose (table II) until the seventh week, while five out of the 15 in the ninth week, and two out of 13 in ninth month, showed agglutinins to a low titre. Even such

TABLE I

	Number under observation	Height of responses	Interval after which obtained	REMARKS
Group I. Oral vaccine, bilivaccine (La Biotherapie Lab., Paris).	29	T. 25 B. 25	9th week	No systemic response of any kind.
Group II. Oral vaccine, typhoral (Bayer).	29	T. 50 A. 25	1st week	No systemic response of any kind. Only two out of 29 showed agglutinins during the first week.
Group III. Subcutaneous inoculation, tri-valent TAB vaccine (Guindy).	27	T. 400 B. 50	1st week	Everyone of them showed mild local general reactions after the injections but the reactions were so severe after the second that six of them had to be placed off-duty.
Group IV. Special	4	T. 100	5th week	No systemic reaction of any kind although three times the advocated dose was administered perorally.

TABLE II

Summary of the response in group I

	Weeks						Months	
	1	2	3	5	7	9	9	12
Number examined	29	27	25	24	16	15	13	14
* Number positive	..	..	..	..	..	5	2	..
Number negative	29	27	25	24	16	10	11	14
B. typhosus (1 in 25).	..	..	..	..	..	4	2	..
Para A	..	..	..	..	..	..	..	..
Para B	..	..	..	..	..	1	..	..

\*Signifies number positive for B. typhosus, para A or B individually or in combination from 1 in 25 and above.

titres were not obtained at the end of a year, but the special group of four (table IIA), who received three times the advocated dose of the vaccine, showed agglutinins to B. typhosus for

varying titres from 25 to 100 commencing from the fifth week, and maintained that level till the end of 12 months. This signifies a better response when doses larger than those advocated are given. Further observations on a larger number of cases are required to confirm this result.

TABLE IIA

Summary of the response in group IV

	Weeks				Months	
	1	2	3	5	9	12
Number examined ..	4	4	4	4	4	2
* Number positive ..	..	..	..	4	4	2
Number negative ..	4	4	4	..	..	..
B. typhosus (1 in 25)	..	..	..	4	4	2
Para A ..	..	..	..	..	..	..
Para B ..	..	..	..	3	..	..

\*Signifies number positive for B. typhosus, para A or B individually or in combination from 1 in 25 and above.

Table III indicates the result of the group treated with oral vaccine (typhoral) and it will be seen that at the end of a week two out of 38 examined showed agglutinins for B. typhosus to titres of 25 and 50, while at the end of nine months 11 out of 18 showed agglutinins for B. typhosus and in some cases for paratyphoid A and B. These were still present at the end of 12 months.

TABLE III

Summary of the response in group II

Time interval	1st week	9th month	12th month
Number examined	28	18	20
* Number positive	2	11	9
Number negative	26	7	11
Percentage ..	7.1	61.1	45
B. typhosus (1 in 25 and over).	2	11	9
Para A (1 in 25 and over).	..	2	..
Para B (1 in 25 and over).	..	2	3

\*Signifies number positive for B. typhosus, para A or B individually or in combination from 1 in 25 and above.

The response of the group subjected to subcutaneous inoculations is given in tables IV and IVA. The agglutinins appeared from the first week onwards and continued to be present right through to the end of the year. The percentage of response ranged from 56.5 to 76.9 which is a little less than that quoted by Dakeyne (1915). The duration of the response and the height of the titres reached varied considerably. The highest agglutinin titre reached was 1 in 3,200 for B. typhosus in the third week, which however fell very rapidly to 1 in 400 in the fifth week.

The total number showing positive response over a period of one year was however large, thus confirming the observations of Dakeyne (1915).

TABLE IV

*Summary of the response in group III*

	Weeks					Months	
	1	2	3	5	9	9	12
Number examined	25	27	26	26	23	20	18
* Number positive	18	19	20	19	13	14	13
Number negative	7	8	6	7	10	6	5
Percentage ..	72	70.4	76.9	73.1	56.5	70	72.2
<i>B. typhosus</i> (1 in 25 and over).	18	19	20	19	11	14	11
Para A ..	..	..	..	2	3	3	1
Para B ..	1	1	..	3	6	1	3

\* Signifies number positive for *B. typhosus*, para A or B individually or in combination from 1 in 25 and above.

TABLE IVA

*Showing the variation in and height of titres obtained at the various periods in group III*

	Weeks					Months	
	1	2	3	5	9	9	12
<i>B. typhosus</i> titres—							
1 in 25 ..	1	..	..	7	..	4	4
1 in 50 ..	2	4	3	4	1	5	5
1 in 100 ..	..	1	4	2	6	2	2
1 in 200 ..	10	3	5	5	3	3	..
1 in 400 ..	5	5	5	1	1	..	..
1 in 800 ..	..	3	1	..	..	..	..
1 in 1,600 ..	..	3	1	..	..	..	..
1 in 3,200 ..	..	..	1	..	..	..	..
Para A titres—							
1 in 25 ..	..	..	..	1	2	3	..
1 in 50 ..	..	..	..	1	1	..	1
1 in 100 ..	..	..	..	..	..	..	..
Para B titres—							
1 in 25 ..	..	1	..	1	3	..	3
1 in 50 ..	1	..	..	1	2	1	..
1 in 100 ..	..	..	..	1	1	..	..

It will be observed that the response for agglutinins was obtained from the sera of the individuals subjected to both oral and subcutaneous vaccination, but the response with the usual dose of vaccine was greatest in the inoculated as against the orally vaccinated.

The earliest period of the appearance of the response for agglutinins was five weeks in the orally vaccinated, if we exclude the two who responded a week after the administration of typhoral, while the response after the inoculation was positive after the first week and continued right through the year. This is quite

consistent with the observation of Park (Kolmer, 1923) as the antigenic action of orally administered vaccines can only come into play after absorption, while the antigens are introduced directly into the vascular system in inoculation.

Although neither the short interval before the response, nor the high titres obtained after oral vaccine, as noted by Hoffstadt and Thompson (1929), were observed in this series, they correspond with the observation of Giglioli (1933), who could not find any response for agglutinins from the fifth to 15 days, following oral administration of vaccine.

In all the individuals of the various groups, the response for typhoid organisms was more than for either para A or B, as observed by the previous authors. It was intended to continue these observations for a longer period and note the increase in response, if any, after the additional administration of an oral vaccine to the inoculated group, after the original titre had started to wane, but the exigencies of service have prevented me from continuing the work.

### Summary

1. The agglutinin response with oral and subcutaneous inoculation of typhoid and paratyphoid A and B vaccines were tested in a group of 89 individuals.

2. Agglutinins to a titre of 1 in 50 or 100 appeared as a rule in the case of the orally vaccinated only from the fifth week onwards and the titres remained low throughout the period of observation.

3. There appears some evidence that an extra dose of oral vaccine leads to a better production of agglutinins, as evidenced by better response when larger doses than those advocated are given. A larger number of cases should however be tested to confirm this observation.

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# Indian Medical Gazette

APRIL

## COORDINATION OF THE MEDICAL SERVICES

THE evolution of the practice of medicine throughout the ages provides a most interesting subject for study. For the moment we will consider it as a continuous process, forget the hiatuses, and ignore geographical considerations. Primitive man, like the dog to-day, probably licked his sores and when he was constipated ate grass, on the one hand, and, on the other, he instinctively fled from association with the sick and avoided poisonous plants, thereby practising both medical relief and prevention. Man became gregarious, and to save him from threatened extinction, as a result of epidemic disease, his most successful leaders became sanitarians and produced religio-sanitary codes, such as the Laws of Moses. The thought was for the herd, not for the individual, whether the leader were a sympathetic champion of the people or a despotic tyrant. Medical treatment was practised by the individual or the mother of the family on lines which she in turn had learnt from her mother. Specialization then appeared in the herd and those who could afford it paid others to treat them, but for the mass it was still home treatment and the Laws of Moses. From this system developed the physician and the surgeon, and, as man became more democratic and the individual more articulate, louder became his demand that his sufferings and those of his family should be relieved; the insistent demand of the half-educated masses was, and still is, for medical relief, and, the laws of supply and demand coming into operation, medical science, which by this time may be said to have been born, adopted as its highest aim the treatment of the sick.

But there were those amongst the more liberally educated who had a wider vision. The Laws of Moses, or their equivalents in other countries and amongst other peoples, had for the most part become unintelligent dogma, for they were usually distorted and even at their best they had not changed with changing circumstances. Disease, it was realized, was not the result of the anger of the Gods, but in many instances of the foolishness of man, the adjective 'preventible' became attached to a number of diseases, and King Edward VII said 'if preventible, why not prevented'. The more the matter was gone into, the longer became the list of preventible diseases, and the idea that all

diseases might be preventible—if only we knew how to prevent them—gradually began to take shape. This provided medical science with a new outlook and its highest aim ceased to be the treatment of the sick—which is only temporizing in the event of failure—and became the final banishment of all human disease.

In medically-advanced countries, when the child gets measles or his father cuts off his hand with a circular saw, not only will the physician prescribe for the child or the surgeon attend to the man's stump, but the medical officer of health will find out where the infection came from and if necessary close the local school, or the industrial hygienist will want to know why the accident occurred; he will not be content with the reason that the man broke certain regulations designed to protect him but he will enquire into the psychology of the man's actions and into such details as to whether it was fatigue or the monotony of his work that led to his carelessness.

This preventive medicine is too idealistic to stir the imagination of the masses; the restrictions that are entailed are irksome and, without the appeal of religious mysticism, often appear as senseless encroachments on man's liberty, even if they are not contrary to his religious principles, which they frequently seem to be, so that in these democratic days prevention usually has to take second place to medical relief, at any rate on the political platform. Another, perhaps more serious retrograde influence is to be found in the fact that this new spirit has not yet permeated the old established system of medical education, with the result that the doctor that is turned out to-day is not yet fully imbued with the preventive outlook; the public health diploma is looked upon as a necessity only for those who wish to specialize in preventive medicine, whereas it would be more logical if the qualifying examination required a knowledge of the general principles of medicine and a thorough training in preventive practice, leaving the more practical aspects of medicine, surgery, midwifery, and other subjects to those who wished to specialize in treatment. This may perhaps appear to be going a little too far; nevertheless the logical outcome of the evolutionary movement in medical practice must be prevention.

Let us see how these evolutionary changes have been interpreted in recent years in India. At the beginning of the century the practice of scientific medicine in the rural districts in India was represented almost solely by the government hospitals and dispensaries, staffed by assistant surgeons and sub-assistant surgeons who were under the district medical officer, or civil surgeon as he was usually called, and the civil surgeons of the province in their turn came under the surgeon-general or inspector-general of civil hospitals. The civil surgeon was also *ex officio* district sanitary officer, but his activities were

mainly directed towards the hospitals and dispensaries, and for the crying needs of environmental hygiene he had neither the encouragement, official or unofficial, nor the inclination, or, if he had had these, neither the knowledge nor the power to do anything. That this was a very unsatisfactory state of affairs was appreciated, and probably the only suitable measure in the circumstances was adopted; a separate department with a separate budget was created in each province and placed under the charge of a sanitary commissioner. These sanitary commissioners, afterwards called directors of public health, had no clearly-defined duties, but in course of time they developed these, and the staffs with which they carried them out, in different ways in different provinces; the work they had before them was boundless, and their activities were only limited by their budget allotments and their personal energies.

There was ample work for both of these departments and there seemed little chance of their interests clashing or of their work overlapping and being duplicated, as long as the public health department concerned itself with strictly environmental hygiene, but it was impossible to continue to take this narrow view of their duties and the first suggestion of overlapping appeared in connection with certain diseases in which treatment is an essential part in the scheme of prevention, *e.g.*, kala-azar (in the present state of our knowledge), tuberculosis, and leprosy. Maternity and child welfare provides another example; until recently a subject neglected by both departments, there seems a danger that it will provide the site for a water-hammer-like clash as both departments meet in the vacuum. Or, perhaps to take a more optimistic point of view, it will form the

point of contact which will extend into a broader line of junction and a possible eventually-complete fusion between the two departments. Elsewhere in this number will be found the opening address of the director-general of the Indian Medical Service at the Delhi Maternity Services Coordination Committee; in this address he has stressed the danger and the futility of this overlapping and has pointed out how easily it can be avoided.

We have said that this division of the departments was probably the best measure that could have been adopted in the circumstances, but had greater foresight been displayed at an earlier date the circumstances would not have arisen. One of the greatest disadvantages of the present system is that it creates in the minds of the laity the impression that in medical science there is a duality of purpose, whereas nothing could be further from the truth; no amount of friendly collaboration will nullify this impression.

We believe that the time has passed when this artificial division can serve any useful purpose, and that the next move must be the unification of the direction of the civil medical services. We do not suggest that the reform is an urgent one; on the contrary, we do not believe that there are yet available sufficient men with the necessary wide experience from whom the directors of medical services in the provinces must be selected, for the sanitary outlook and sanitary experience will be essential qualifications. The present system has worked well for many years and with a spirit of willing co-operation between the heads of the respective departments in the different provinces, it will probably continue to do so, but eventually, as medical science has only one aim, unification of directorate is inevitable.

## Special Articles

### HÆMATOLOGICAL TECHNIQUE

#### PART III

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#### (5) Enumeration of reticulocytes

RETICULOCYTES, or reticulated erythrocytes, are young red cells; they represent the stage just after the cells have lost their nuclei and before they are fully mature. They are expressed as a percentage of the red cells; their percentage incidence gives information as to the activity of the red blood cell formation at the moment.

The reticulation may appear as a net-work over the whole cell, as a collection of discrete rods, or as granules. These are not shown by ordinary Romanowsky stains and a special supravital staining method is necessary to demonstrate the reticulation.

*Staining methods.*—Various dyes have been tried for staining reticulocytes, but brilliant cresyl blue has been found to be the best and it is now used universally. Although brilliant cresyl blue is the dye of choice, a number of different methods of using it have been suggested. Methods for reticulocyte staining may be classified in the following groups, in all of which scrupulously clean and polished slides and



coverslips without any scratches should be used\* :—

A. Methods in which a thin film of the dye is dried on the slide or coverslip and the blood added later.

B. Methods in which the blood is mixed with a solution of the dye.

With either method (i) a dried smear may be made, or (ii) a wet coverslip preparation.

*Special apparatus required [for method of choice, B (ii)]*

Polished slides.

Clean coverslips (preferably 22 × 40 mm.).

Cresyl-blue solution 1 per cent in 0.85 per cent sodium chloride.

Capillary pipette.

Rubber teat.

Vaseline or paraffin.

Gas or spirit lamp.

Ehrlich's eyepiece (or some means of limiting the microscopic field).

Microscope.

*Additional requirements for other methods*

Surgical pricking needle or 'blood gun'.

Alcohol, ether, and cotton-wool.

Cresyl-blue solution 1 per cent in absolute alcohol.

Wide-mouthed glass bottle

Specimen tube

Filter paper

Leishman's stain

Distilled water

} A (i) and (ii).

} A (ii) and B (i).

#### *Method A*

To prepare slides or coverslips proceed as follows :—

Make a 1 per cent solution of brilliant cresyl blue in absolute alcohol and keep it in a well-stoppered bottle. The slide may be prepared by one of the following methods :—

(a) Take a polished slide, heat it a little over a flame and put it on a flat even surface. With a capillary pipette take some brilliant-cresyl-blue solution from the stoppered phial and put a drop on the middle of the slide. If the slide is clean and it is on an even surface, the stain will spread concentrically and will be distributed in a uniform manner. The stain will dry in a minute or so; the slide is then ready for use.

(b) Put some stain in a wide-mouthed glass bottle. Warm a polished glass slide by passing it through a Bunsen flame, and holding it in a pair

\* *Slides.*—These should be cleaned and polished in the following way :—

(i) Only new slides should be used. Put the slides in a glass jar containing spirit. Keep them soaked in spirit for over 24 hours.

(ii) With a pair of forceps take out one slide at a time, allow the spirit to drain off the slide, and then flame it over a spirit lamp or gas burner.

(iii) Polish well one side of the slide with jeweller's rouge, using a soft cloth. Mark the polished side with a glass pencil and keep it in a dust-proof slide box.

*Coverslips.*—Keep the coverslips in a wide-mouthed glass jar soaked in spirit. Just before use, with a pair of fine forceps, take out one coverslip at a time, allow the spirit to drain off, flame them over a spirit lamp or gas burner, clean with a soft cloth and keep them covered in a small Petri dish till they are wanted.

of forceps dip it vertically into the jar of the dye up to three-quarters of its length. Take it out, allow the excess of stain to drain back into the bottle, and, before it is dry, put it in an upright position inside a specimen tube at the bottom of which a piece of blotting paper has already been placed. Put in the cork and allow it to stay over-night; take it out, mark one side with a glass pencil, and wipe the stain from the other side of the slide with a moist cloth; it is then ready for use.

Slides prepared in either of these ways may be kept for a long time in a dust-proof slide box and used when required.

(i) To prepare a dried smear, only slides prepared by the second method are suitable.

Put a drop of blood, oxalated or from the finger, on one end of a prepared slide and draw a very thin smear across the stained surface of the slide in the usual way—the use of a haemocytometer coverslip as a spreader facilitates the drawing of a thin smear. Slides prepared in this way may be counterstained with any of the Romanowsky stains in the usual way.

(ii) To make wet coverslip preparations, slides prepared in either of the above methods may be used.

Put a drop of blood, oxalated or from the finger, on the stained surface of a prepared slide, gently place a coverslip on the drop of blood, avoiding air bubbles as far as possible. If the drop of blood is not too big, it will spread uniformly under the pressure of the coverslip, but, in case it does not do so, apply very gentle pressure with the tip of the finger, so that the blood spreads evenly, but on no account should the coverslip be pressed hard, as some of the cells may be ruptured. Ring the coverslip round with hard paraffin by dipping a match in melted paraffin and stroking it on to the slide at the junction of the slide and coverslip.

#### *Method B*

In this method a small amount of blood is mixed with a quantity of dye in some definite proportion.

(i) Method of Osgood and Wilhelm (1934).

Put 0.5 c.cm. of 1 per cent brilliant-cresyl-blue solution in 0.85 per cent sodium chloride into a small test-tube on a rack. Add an equal quantity of oxalated blood from a well-shaken flask. Mix well and allow the mixture to stand for about two minutes. Rotate the tube between the hands to get an even mixture.

Withdraw a little of the mixture with a capillary pipette and put a drop at one end of a polished slide. Make a thin smear and, when it is quite dry, counterstain with Leishman's stain in the usual way. The slide is now ready for examination for reticulocytes. A differential count of the leucocytes can also be done at the same time.

(ii) Modification of the above method. This is the method of choice.

Prepare a mixture of cresyl blue and oxalated blood as in the above method. With a capillary pipette take out a little mixture and put a small drop at about the centre of the polished side of a clean slide. Apply a clean coverslip on the drop of the mixture, when, under the pressure of the coverslip, the mixture will spread evenly; but, in case it does not do so, very gentle pressure with the tip of the finger may be applied over the coverslip. The preparation is then sealed with vaseline or paraffin and is ready for examination for reticulocytes only.

### *Counting the reticulocytes*

Slides prepared by any of the methods described above are first examined rapidly with a low power (2/3rds objective), and a portion of the slide is selected where the cells appear discrete and these are not too many in one field. This portion of the slide is now examined with the 1/12th oil-immersion lens. The total number of red cells in the field and also the number showing reticulation are counted. The use of an Ehrlich's eyepiece, or a piece of metal with a square hole in it placed inside the eyepiece to narrow down the field, greatly facilitates the counting. Altogether one thousand red cells are counted in a more-or-less normal case, but if the count is high, 5 per cent or more, 500 red cells is sufficient; the number of cells showing reticulation is noted, and from this the number of reticulocytes per 100 red cells is calculated.

A Veeder counter, or some similar device, is useful here; one counts the red cells, and each time a reticulocyte is encountered clicks the Veeder. When a thousand red cells have been counted, the number on the Veeder is read.

In the absence of an automatic counter, a pencil and paper must be used, for it is a mistake to try to keep two sets of figures in one's head.

### *Comment*

Osgood and others have shown that divergent results are obtained with the different methods in use. They obtained the best results with the method described by them, which has the additional advantage that a differential count of the leucocytes can also be done in the same preparation. We have, however, found that the modified Osgood method, which is the routine procedure in our laboratory, has given even better results in our hands than the original method. With the modified method all the reticulocytes stain very well and there is no clumping nor overlapping of the cells; thus, the counting is very much facilitated. With the original method a number of cells appear broken, more so in the case of anæmic blood, and the cells are less discrete. The percentage of reticulocytes appear to be slightly lower in the original than in the modified method. In a small number of cases where the counts were done by both methods, 5.16 per cent reticulocytes were found by the original method, against 5.98 by the modified method.

On account of the divergent results obtained by the different methods in use, for comparative studies a uniform technique should be adhered to in the enumeration of the reticulocytes, not only by one group of workers, but by all, so that the results of different workers will be comparable.

The modified Osgood method, described above, is simple and as it appears to be superior to the other methods in many ways, we recommend it as the method of choice for the enumeration of reticulocytes.

### *Normal values*

It is unnecessary to quote the figures of numerous observers regarding the normal percentage of reticulocytes. When, in a healthy individual whose red cells are at the normal physiological level, the hæmopoietic and hæmolytic tissues are functioning normally, the number of reticulated reds cells reaching the peripheral blood is less than one per cent of the total red cells. The normal range is usually given as 0.1 to 1.0 per cent. The present writers found a mean percentage of  $0.67 \pm 0.37$  in a series of 50 city-dwelling Indian males, with a range from 0.2 to 1.4, and  $0.37 \pm 0.27$  amongst 122 women. On the other hand, for Assam tea-garden coolies the mean was  $2.17 \pm 1.92$  and the range 0.1 to 10.8 per cent. It is probably true to say that reticulocyte counts in man of over 1.0 per cent are evidence of some unusual stimulation to the hæmopoietic system, though they may be encountered in an apparently healthy individual. In our Assam coolie series, we accepted these findings of unusually high reticulocyte percentages, associated as they were with a low hæmoglobin percentage, as evidence of some abnormality of the erythron in the individuals concerned.

### *Significance of reticulocytes*

Whenever the hæmopoietic system meets an extraordinary demand for red blood cells, the reticulocyte percentage will rise, but the reticulocyte rise will *not* be maintained until the deficiency of the red cells has been made good.

For example, if a healthy individual loses a large quantity of blood, there is an immediate steady rise in the reticulocyte curve which reaches its maximum and falls to normal again within a few days, whereas it will probably be a few weeks before the loss of blood cells is made up.

Similarly, in deficiency anæmias, when the deficient substances, e.g., hæmopoietin in pernicious anæmia and iron in iron-deficiency anæmia, are supplied, the hæmopoietic tissues in the bone marrow are now enabled to meet the demand for red cells, and there is a rise in the reticulocyte percentage that starts within two or three days and reaches its maximum within five to ten days, after which it falls as fast as it rose.

This reticulocyte rise gives a valuable indication that a deficiency has been made good.

A third example is in toxic aplastic anæmia, where a toxin is depressing the function of the bone marrow. In this case there may be no reticulocytes at all to be found in the peripheral blood, but once the toxin is neutralized, or otherwise ceases to exert its toxic effect, the hæmopoietic tissues will start to function properly, reticulocytes will appear in the blood, their percentage will rise to a maximum within a few days and will fall again to the normal level, but in the absence of any further intoxication the red cells will continue to increase until they reach their normal level.

It should be emphasized that whilst a reticulocyte crisis, as this sharp rise is called, is evidence that the hæmopoietic tissues are functioning effectively, a fall of reticulocytes to the normal level does not indicate any cessation of this functioning, but on the contrary it indicates that red blood cell formation is being carried on in an orderly manner.

In true hæmolytic anæmias, there is a constant reticulocytosis, as not only will the anoxæmia stimulate erythropoiesis, but there is a second source of stimulation in the debris of abnormal hæmolysis which has to be disposed of by the reticulo-endothelial tissues.

A constant reticulocyte count of 5 to 10 per cent or higher is evidence of excessive hæmolysis, and in a hæmolytic anæmia the return of the reticulocyte count to normal is usually evidence that the excessive blood destruction has ceased.

#### *Reticulocyte crises*

The extent of the reticulocyte response is governed mainly by the original level of the red cells in the anæmic state. For example, in a case of pernicious anæmia the rise in the reticulocyte percentage after the same adequate dose of liver extract may be as high as 55 per cent or practically negligible, according to whether the red cell count was 500,000 per c.mm. or 3,000,000 per c.mm. before treatment. Doubling the dose of liver extract would make no difference to the height of the reticulocyte response, but reducing it to an inadequate dose would. Therefore, in pernicious anæmia, if one has a chart showing the expected reticulocyte response, one can judge whether or not the dose of liver extract given was an adequate dose. We have given a chart here, not so much for practical use as pernicious anæmia is rare in India, but to demonstrate this point.

In iron-deficiency anæmia, the response to adequate iron therapy is also proportionate to the degree of the anæmia, but in this case the reticulocyte count does not respond with the same mathematical precision.

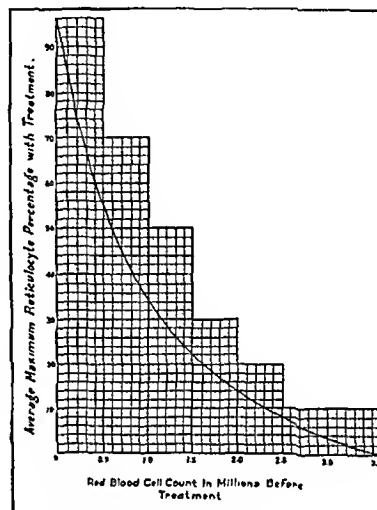
#### (6) Enumeration of thrombocytes

Thrombocytes, or blood platelets, are colourless or slightly bluish bodies, spherical, ovoid, or pear-shaped, and are usually about one-third

of the diameter of a red blood cell, but they may be larger, especially in pathological conditions.

No method of enumeration of blood platelets is entirely satisfactory, as platelets tend to form clumps and to stick to any foreign surface with which they may come into contact. However, with careful technique, counts sufficiently accurate for practical purposes are not difficult to obtain. The principal point to be remembered in the platelet count is that manipulation of the sample of blood should be avoided, and, if possible, the blood should be taken directly on to the counting slide.

CHART



Riddle's chart for calculating the maximum reticulocyte response expected in pernicious anæmia with adequate therapy.

The platelet count is expressed as a number per cubic millimetre of blood. There are several methods for estimating the number of platelets; these fall under the two main heads, the direct and indirect methods.

#### *Apparatus required [for method of choice, B (i)]*

As in the reticulocyte count.

#### *Additional requirements for other methods*

*For method A.*—Red blood cell pipette.

Sodium citrate 2 per cent solution (fresh and sterilized).

Counting chamber with Neubauer ruling and coverslip.

*For method B (ii).*—Magnesium sulphate 14 per cent solution.

**A. Direct method.**—In this method the number of platelets per cubic millimetre is calculated without any reference to the red blood cell count.

Prick the finger with a sharp surgical needle and with a red-cell pipette draw blood up to the 0.5 mark and dilute it with fresh sterile 2 per cent solution of sodium citrate, up to the 101 mark. After gentle shaking, put a drop in the counting chamber, wait 3 to 4 minutes to allow the platelets to settle down, focus the light carefully, and count with the high power all the platelets in one square millimetre area. The

number of platelets per cubic millimetre of blood is then calculated in the usual way.

**B. Indirect method.**—As in the enumeration of the reticulocytes, the platelets are at first expressed as a percentage of the red cells calculated from the number of platelets observed in counting one thousand red cells. The number of platelets per cubic millimetre can then be calculated from the total red cell count, which must be done at the same time. Of the many indirect methods advocated, the following two methods have given consistently good results in our hands :—

(i) Clean the tip of the finger first with soap and water, and then with alcohol and ether, and

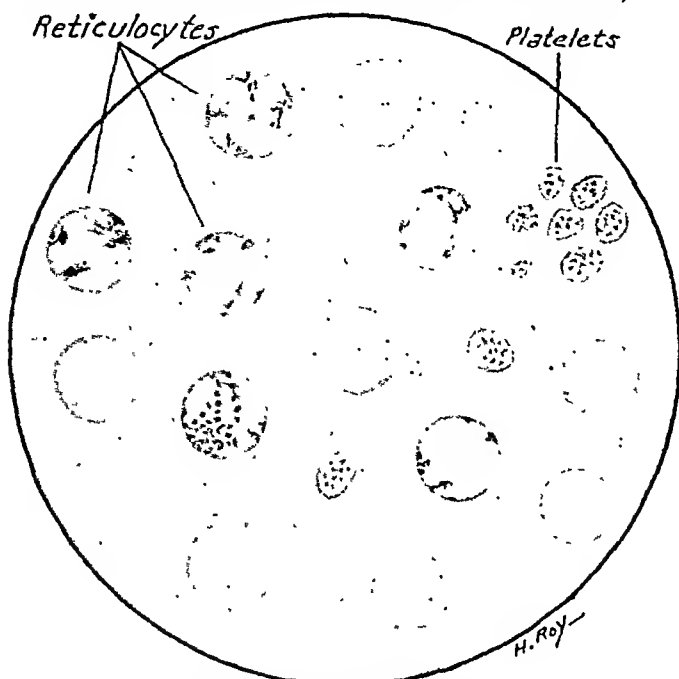


Figure showing six reticulocytes, seven mature erythrocytes, and nine platelets.

apply a thin layer of sterilized vaseline over it. Prick the finger with a blood gun or sharp pricking needle through the thin layer of vaseline. As the blood comes out, touch the uppermost portion of the blood drop with the centre of a 22 × 40 mm. coverslip. Place the coverslip on a dried cresyl-blue-stained slide prepared by method A, (a) or (b), as described for the reticulocyte count. With very gentle pressure try to obtain as uniformly spread a film as possible, and finally seal the sides of the coverglass with vaseline or paraffin.

(ii) Clean the tip of the finger as above. Balance a drop of 14 per cent solution of magnesium sulphate on the back of the finger just above and to one side of the nail groove. Make a small puncture through the drop. The drop of blood should be such that the resultant blood mixture is about 1 in 20. Mix rapidly with a paraffined\* capillary pipette.

\*Platelets do not adhere to a paraffined surface, so that if glass is covered with a thin layer of paraffin the platelets do not tend to adhere to it. The pipette is prepared by drawing hot melted paraffin wax through it; a thin layer of paraffin will adhere to the glass when it cools.

Transfer the blood mixture to clean slides, make very thin smears and stain with Wright's or Leishman's stain.

The coverslip preparation (i), or the slide (ii), is examined with an oil-immersion lens. A small rectangular field is more convenient for counting than a big circular one (v. s.). Note the number of platelets seen in counting 1,000 red cells.

Successive fields from the different areas of the smear should be examined so as to eliminate, as far as possible, the error from uneven distribution. The red cell count is done in the usual way.

By a simple calculation the total number of platelets per c.mm. may now be ascertained. Thus, if the total red cell count is 5,000,000 per c.mm., and if  $x$  be the number of platelets counted against 1,000 red cells, then  $\frac{x \times 5,000,000}{1,000}$  or  $x \times 5,000$  is the total number of platelets per c.mm.

*Example.*—Total red blood cells = 4,500,000 per c.mm.  
Number of platelets counted against 1,000 red cells = 50.  
Therefore:—

$$\text{Platelets per c.mm.} = \frac{50 \times 4,500,000}{1,000} \text{ or } 50 \times 4,500 = 225,000.$$

The enumeration of the platelets by the indirect method, though more laborious and time absorbing, as a total red cell count has also to be made, is nevertheless much superior to the direct method. Results obtained by indirect methods, especially by method (i), are always higher than those of the direct method, as there is very little contact with foreign surfaces.

#### Normal values

The figures given by different writers vary considerably. This variation is undoubtedly due to some extent to the differences in the methods adopted for counting them, but there are considerable variations in the platelet counts done at different times by the same method in the same individual.

Whitby and Britton (1939) in Great Britain give the range as 250,000 to 500,000 per cubic millimetre and Gram (1920) in America as 280,000 to 540,000 with the average at 350,000. The present writers found  $369,000 \pm 248,000$  in Calcutta and  $423,000 \pm 343,000$  in Assam; in the latter series there were a number of so-called normal individuals with platelet counts of over a million and a half.

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## DRUG MANUFACTURE IN INDIA DURING PEACE AND WAR\*

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### DEMAND FOR CHEAP MEDICINE

As chairman of the Drugs Enquiry Committee, I realized that the root cause of the traffic in adulterated drugs is traceable, on ultimate analysis, to the demand by the people of this country, for cheap medicines. The western system of medicine is extending rapidly among the masses, and with it the use of medicinal drugs is going ahead. As many cannot afford to buy drugs of good quality on account of their high price, the demand for and sale of cheap drugs of poor quality and strength has been flourishing. Some unscrupulous manufacturers and dealers have not been slow to exploit this demand, and in the absence of restrictive laws certain classes of manufacturers and dealers, both in India and abroad, have successfully flooded the market with inferior products. The only remedy for this state of affairs lies in the organization of the drug industry in our country. It is only then that we shall be able to satisfy the conditions which might be prescribed by properly considered drug-control legislation, and to put on the market standard goods which the people need and which will suit their purchasing capacity.

In the report of the Drugs Enquiry Committee (1930-31), the difficulties of the local manufacturers in this country were fully discussed. The evidence disclosed the various disadvantages from which they suffered and which have hindered progress. The diversity of excise regulations for spirituous preparations was referred to, and during recent years there has been a certain amount of improvement in this direction. The difficulties of getting crude vegetable drugs have also decreased during recent years. Progress, I believe, has been made in connection with the high railway freight for transportation of raw material and medicines manufactured in India. The greatest difficulty of the honest manufacturer is competition with dealers who import cheap drugs of low standard and with small manufacturers in this country, who purposely turn out inferior products. Legislation, in the form of a Drug Control Bill which will be enacted in the near future, will, I have no doubt, put an end to this state of affairs. The drug industry in India stands on very much firmer ground and under more favourable conditions than even a decade ago. The manufacturers of drugs are, therefore, now in a very much better position to cope with the conditions which have

been created by the present war than they were in 1914 and during the period of the last war.

### PRESENT STATE OF DRUG INDUSTRY

Let us now examine what is the position with regard to the manufacture of medicinal preparations at the present time in India. Although no reliable statistics are available, from the knowledge I have of the drug industry in India, I have reason to believe that medicinal drugs manufactured in this country may at the present time be estimated at not less than 30 to 40 per cent of those imported, i.e., of the total figure Rs. 2,59,34,000 of imports, as shown by the sea-borne-trade returns of British India during 1936-37. There are probably less than a dozen of the larger firms of drug manufacturers in this country who turn out medicinal preparations on a large scale. Most of them manufacture medicinal drugs, pharmacopœial and otherwise, proprietary preparations, and toilet products, in many cases from basic material largely imported from abroad. So far as basic chemicals are concerned, the produce at present is mainly confined to small quantities of acids and a few of the common chemicals. Attempts are, however, being made to improve this state of affairs and to start the manufacture of heavy chemicals, such as alkalis, acids, chlorine products, etc., in India, but as far as I know these schemes have not fully matured, therefore at present we have to depend on imports from abroad for most of these products. Some Indian firms have lately started the manufacture of patent foods, but much remains to be accomplished before we achieve the standard of many of the imported products. Even such an essential product as glucose has not yet been manufactured in this country.

Besides these large firms, there are a very large number of small firms, some of which manufacture standard products, but many of which turn out preparations which are not above suspicion. Some import products in bulk from concerns of doubtful reputation abroad, bottle them, and sell them to the public. Others obtain concentrated extracts and dilute and label them with their own names before sale. The capital of all the drug manufacturing concerns in India, large and small, put together would not amount to much more than 60 or 70 lacs of rupees. In the absence of any drug control, all these manufacturers appear to be making handsome profits in spite of the fact that many are poorly equipped and inefficiently staffed.

### DRUG INDUSTRY IN WAR TIME

The outbreak of war and the difficulties of getting regular supplies of drugs and essential medicinal chemicals have profoundly affected the drug market in this country. This is natural as India has been and still is largely an importing country in the matter of her supply of drugs. While a large proportion of the drug imports come from the United Kingdom, considerable

\* The résumé of an address at the opening of the All-India Conference of Chemical and Pharmaceutical Manufacturers, on the 6th November, 1939.



quantities of these and certain basic chemicals necessary for drug manufacture came from Germany and other enemy countries. As a great proportion of these have for the time being been cut off, it is important to see how they could be replaced, (1) by manufacture in this country, and (2) where this is not possible by importation from the United Kingdom and neutral countries.

So far as the possibility of manufacture of India's drug requirement in India is concerned, it can now be said with confidence that the indigenous drug industry has progressed considerably; it is now on much firmer ground, and is in a position to supply a large number of the drugs and other medical supplies in common use. It is to be greatly regretted that for many of the essential basic chemicals, solvents and synthetic remedies India is still dependent on supplies from abroad.

#### A REVIEW OF INDIA'S POSITION WITH REGARD TO DRUG SUPPLY

The drug industry in this country may be classified under five headings:—

##### I. *Manufacture of pharmaceutical preparations, essential oils, fixed oils, etc.*

So far as the drugs of vegetable origin are concerned, India is fortunately in a much better position than many other countries of the world. India has a wonderful range of materia medica and nearly three-fourths of the drugs mentioned in the British and other pharmacopœias grow here in a state of nature or have been cultivated. Where the pharmacopœial species do not grow, allied species are available which may be used as substitutes. If our resources are properly husbanded and conserved, India could not only be completely self-supporting in this respect but might also be in a position to supply the rest of the Empire with all the raw products that are needed in the preparations of pharmaceuticals. At present, Great Britain draws a fairly large supply of crude drugs from mid-Europe, particularly from areas which are now under German influence. These will presumably be cut off to a large extent and Indian sources may be of use in meeting such deficiencies as might occur.

*Essential oils.*—With regard to essential oils, India has the *basic materials* from which ajowan, caraway, chenopodium, cinnamon, coriander, cardamom, rose, sandal wood, turpentine, etc., can be produced, but others she imported chiefly from central European countries. With the exception of sandal-wood oil, essential oils have not hitherto been distilled in large quantities on proper scientific lines in India, but there is no doubt that this industry could be successfully developed in a very short time.

*Fixed oils.*—Almost all the fixed oils used in medicine, e.g., almond oil, arachis oil, castor oil, hydnocarpus oil, and oils of linseed and sesame are available in India. Olive oil may be easily

replaced by arachis oil. Purified medicinal castor oil is now imported as cold-drawn oil and is seldom manufactured in India, though the ordinary oil used in hospitals and dispensaries is produced in this country. There would be no difficulty in preparing the purified oil used in medicine in sufficient quantities for the needs of India and the Empire.

##### II. *Manufacture of alkaloids and other active principles from vegetable drugs.*

*Alkaloids, etc.*—Of the alkaloids commonly employed in therapeutics, India can produce atropine and its salts, caffeine and its derivatives, emetine, ephedrine, morphine, codeine, quinine, strychnine, etc. Strychnine is already being manufactured in large quantities and is exported to Australia. Caffeine can be manufactured if tea fluff (dust) is made available to the *bona-fide* drug manufacturers by the Indian tea industry at a reasonable price. Morphine and its derivatives including codeine are being produced at the Ghazipur opium factory. Large supplies of ephedra and belladonna are available and ephedrine and atropine can be produced in almost any quantity. Some of these industries could not develop during peace time, owing to keen foreign competition and high prices of the solvents which have to be used.

For quinine, both India and the rest of the world will have to depend on the Dutch East Indies for some time to come. India produces a limited quantity of cinchona alkaloids. Between the two plantations at Mungpoo (Sikkim Himalaya) and Neduvattum (Nilgiris), roughly between 65,000 to 70,000 pounds of cinchona alkaloids are produced every year. The total annual expenditure in India at the present time is over 200,000 pounds, so that over 100,000 pounds has to be imported from Dutch East Indies. I have on many occasions urged the extension of Indian plantations, but cinchona plantations take seven to eight years to mature so that for the present emergency India will have to depend on the Dutch East Indies for its supply of cinchona alkaloids.

Ipecacuanha is also being grown in Mungpoo but the supply is small and not commensurate with the demands. This plantation could easily be extended and in the meantime the supplies can be procured from the Federated Malay States, where it grows extremely well. Artemesias grow in Kashmir and in the Kurrum valley, and santonin is manufactured in Kashmir on a large scale and is exported to different parts of the world.

##### III. *Manufacture of inorganic and organic chemicals used in medicine*

*Inorganic drugs.*—The important inorganic drugs used in medical practice are:—boric acid, hypophosphorus acid, salts of ammonium (chloride carbonate), potassium (iodide, bromide, chlorate, permanganate), sodium



(bromide, bicarbonate, iodide, phosphate, salicylate) and magnesium (carbonate, oxide, sulphate). For almost all of these, India depends on foreign supplies at the present time. Apart from alkalies and acids, the most important items required are iodine and bromine. So far as iodine is concerned there is the possibility of securing it from Japan. If Great Britain revives the Scottish Kelp Industry during the war, there is also the possibility of getting at least a partial supply from this source. Bromine will be more difficult and special measures will have to be devised to secure it. Some of the above-named inorganic drugs are already being manufactured in India, but their manufacture entirely depends upon the supply of certain essential basic chemicals and solvents from abroad. Every effort should be made to encourage the production of these basic materials in India.

*Special organic drugs.*—Practically without exception all of the special organic drugs have to be imported at present. The chief source of many of these, such as acetone and acetic acid, acetylsalicylic acid, benzol and benzoic acid, citric and lactic, oleic, tartaric and trichloroacetic acids, ether, ethyl chloride, chloral hydrate, chloroform, hexamine, glycerine, amyl nitrate, urea and lactose, was Germany, though some were also obtained from the United Kingdom and the United States of America. Many of these have been or can be manufactured under emergency conditions in India, provided basic chemicals and solvents are available.

*Metals and organo-metallic compounds.*—For preparations like gold salts, silver compounds, inorganic preparations of mercury (mercurous and mercuric chloride, mercuric iodide), inorganic arsenicals (arsenic tri-iodide and tri-oxide), inorganic bismuth compounds (bismuth carbonate and salicylate) and lead compounds (lead subacetate), India is entirely dependent on foreign supplies at the present time. Many of these compounds could easily be manufactured. Copper salts (sulphate) can be prepared from Indian copper, while zinc, antimony and lead can be obtained from Burma.

The organo-metallic compounds of gold (solanol, sanocrysin, etc.), silver (argyrol, protargol, etc.), mercury (novasurol, salyrgan, mercurochrome, etc.), arsenic (neoarsphenamine, sulpharsphenamin, stovarsol, carbarsone, tryparsamide, etc.), antimony (ureastibamine group, neostibosan group, stibamine glucoside, etc.) are mostly imported at present. Organic compounds of arsenic, antimony and bismuth have been successfully prepared in India, and if research is properly organized most of these compounds could be prepared in this country. Reserve stocks held in India may be sufficient for the needs of the immediate future, but, in the case of a prolonged war, supplies for the population of the country should be ensured and this can only be done by encouraging local manufacture.

#### IV. *Manufacture of biological products including sera, vaccines, gland products, etc., vitamins and food preparations*

*Glandular products including liver extracts.*—There should not be any great difficulty for the supply of these products from the U. S. A. but many of these can be manufactured in India provided the slaughter-houses are run properly and the dissection and separation of fresh glands are done under expert supervision. The question of solvents is also of prime importance in this connection. One or two of the manufacturing houses in Calcutta have produced thyroid, adrenal and posterior pituitary preparations. Some of these have been tested in the Biochemical Standardization Laboratory and have given satisfactory results. There is little doubt, however, that quite a large proportion of India's requirements in these glandular preparations and of products such as testicular and ovarian preparations, insulin, corpus luteum preparations, etc., are at present obtained from abroad. Within the last few years, sex gland preparations are being produced synthetically and are in large demand. Their therapeutic uses are still largely experimental and even if they are cut off, not much difficulty is likely to be experienced. Liver extracts both for oral use and injectable forms can be, and actually are being, prepared in India.

*Vitamin preparations, patent foods and irradiated milk foods and cereal products.*—Vitamin preparations have now established themselves in therapeutics and are being prescribed by a large number of practitioners. Pure vitamin preparations which are largely of synthetic origin are imported and will be difficult to get during war time. The want of these preparations can be largely met by giving natural vitamin-rich foods in suitable quantities.

Cod-liver oil is an important imported product and will probably be difficult to obtain. I have no doubt that it can be replaced by fish-liver oils of India, some of which have a high-vitamin content, if a little more research is carried out in this direction.

Some patent foods and irradiated milk foods are important accessories to medical treatment. These are all imported but fortunately a large quantity of these are obtained from Great Britain and, therefore, at least a partial supply will be possible.

*Biological products.*—Prophylactic and curative sera of all types are being manufactured in India. If the quality of these is controlled by proper standardization, this source could easily be developed to meet all the Indian demands. For this International Standards (toxins, antigens, antitoxins, etc.) have to be regularly supplied to the manufacturers.

#### V. *Surgical dressings, disinfecting fluids, etc.*

Absorbent cotton, gauze, jute, lint, bandages, etc., are being manufactured in India and no difficulty need be apprehended.

Disinfecting fluids of the type of phenol, cresol, etc., are being prepared in very small quantities from coal-tar distillation, but their manufacture could be extended.

#### REQUIREMENT OF DRUG MANUFACTURERS AND DIFFICULTIES IN PROCURING SUPPLIES

I may here briefly refer to some of the difficulties of the manufacturers in connection with obtaining supplies of materials used in the manufacture of medicinal preparations under the conditions which have arisen on account of the war.

A critical analysis of the situation convinces me that the chief difficulty lies in the fact that India does not at present possess facilities for producing certain essential basic materials, such for example as alkalis, acids, solvents, phenol, aniline, iodine, bromine, urea, etc., which may be said to constitute the keystone of the drug manufacturing industry. In the case of some of these, the country lacks the natural resources of these materials, but in most cases their production is dependent on the other associated industries which are non-existent in India at present. I may here give a few examples:—

(a) *Mineral acids.*—Sulphuric acid is the key substance used in the production of many pharmaceutical preparations, as besides being used in the manufacture of alum, sulphates of magnesium, sodium, ammonium, iron, etc., it has other important applications. Its manufacture is at present entirely dependent on the supply of sulphur which is derived from Japan, Italy and America. The consignments from the two former countries have recently ceased, and difficulty has been experienced by some firms in obtaining sulphur. Supplies are, however, maintained from America and no serious shortage need be apprehended. The chief source of sulphur in this country is from iron and copper pyrites of which large supplies are available in Behar and some are even free from arsenic. Attempts are being made to utilize these in the preparation of sulphuric acid.

If sulphuric acid can be produced other mineral acids can be readily manufactured.

(b) *Alkalies, and chlorine and its derivatives.*—The manufacture of alkalies—soda ash, potash, caustic soda and caustic potash—is poorly developed in India and almost the entire supply is imported from abroad. It is a matter of satisfaction to note that attempts are being made to develop the manufacture of both these groups of important chemicals in India and when this is accomplished a great forward step will be taken in the development of drug and other industries in this country.

(c) *Organic acids.*—Almost all organic acids are imported at present and are converted into salts used in pharmacy. Citric acid can be produced in limited quantities from limes and lemons and tartaric acid from tamarind, and this was actually done during the last war. It would be possible to produce salicylic acid from

oil of wintergreen (from *Gaultheria fragrantissima*) and benzoic acid from gum benzene.

(d) *Solvents.*—With the exception of alcohol, practically no solvents are produced on any large scale in this country. This has been attributed to the high excise duty in the case of some of them. Benzol or commercial benzene is in considerable demand, but so far, for various reasons, it has been isolated only by a few firms. This is going to be taken up on a large scale by some of the iron and steel manufacturing firms, but it may take a year or two before the plants are set up and begin to function. Ether is now being produced in India and it should not be difficult to produce petroleum ether which is largely used in the preparation of galenicals and which so far has been imported. Chloroform can be manufactured in any quantity if chlorine or bleaching powder is available.

(e) *Other substances.*—These are but a few examples. Many more of the chemical compounds of arsenic, antimony, bismuth, phosphorus, etc., camphor, urea, aniline, which are mostly imported at present and which could be manufactured in this country, could be cited.

I am convinced that all the different departments of the Government of India are very willing to help everyone concerned in solving the difficulties which have arisen and which are likely to arise on account of the present situation. All they need is a representative organization of the different interests concerned with the manufacture, import and sale of drugs and which would be authorized to deal with the supply department in connection with any difficulties that might arise. This is what is wanted and it is the obvious duty of an Association such as this to help in setting up an organization which will not only deal with the Government, but will take up the question of drug manufacture in India on proper scientific and business lines. I said in the beginning that the root cause of trade in spurious and low-standard drugs in this country is the demand by the people for drugs which they can afford to pay for.

## Medical News

### THE NEED FOR CO-OPERATION IN THE MEDICAL HEALTH SERVICES OF INDIA WITH SPECIAL REFERENCE TO MATERNITY AND CHILD WELFARE

(AN ADDRESS BY MAJOR-GENERAL G. G. JOLLY TO THE DELHI MATERNITY SERVICES CO-ORDINATION COMMITTEE)

THE development and expansion of the spirit of co-operation is one of the greatest needs of our time. Divisions between man and man, whether along racial, national, religious, linguistic or other lines, most of which have existed for ages, seem to have become more prominent in recent years and to obtrude themselves when any serious attempt is made to improve human relations on a co-operative basis.

And yet, paradoxically enough, a genuine desire for co-operation and a realization of the need for it also

seems to be more widespread than ever before. Perhaps it is that with the spirit of co-operation abroad the obstacles real and imaginary stand out more clearly in contrast and the forces of reaction tend to be mobilized in opposition.

The medical profession has not remained immune from the general tendencies. In England the formation of the Ministry of Health after the last war was a much needed piece of reorganization, co-ordinating under one central direction a series of separate health services each of which formerly served a section of the population. A Ministry of Reconstruction pamphlet of 1919 states: 'In the absence of a Ministry of Health the departments concerned with each special section retained and developed their own responsibility by means of independent and watertight machinery, while as every such section of the population overlaps to some degree every other section, the specialized health provision thus established rapidly became full of duplication and overlapping'. In England now the lack of co-operation is not so much between different sections of the official health services as between these official health services and the great body of private practitioners. Possibly the eventual solution may be the formation of a complete medical service for the nation, which in effect would make all practising medical men officials of the State.

Here in India lack of co-operation between official and non-official doctors has not yet made itself very apparent outside the towns because, so far, few private practitioners have settled in the rural areas. What has, however, to be guarded against is a tendency to overlapping and lack of co-ordination within the Government Medical Services. This would be most unfortunate. We are all members of one great profession serving the public, we have a common objective—the health of the people—and, within our geographical boundaries, we work side by side under one Government. Most of you will know the old jest about parallel departments of government being those which correspond indefinitely but never meet. It is with the object of giving the lie to that definition in regard to the medical health services of Delhi Province, with particular reference to maternity and child welfare, that we meet here this evening.

In order to get the picture clear it is necessary to look back at our development.

Some thirty or so years ago the Government Medical Services in the provinces of India were split into two, a personal service dealing mainly with the individual and an environmental service concerned primarily with the community.

Some have called these separated departments the curative and the preventive, but this is clearly a misnomer for it is impossible to draw any clear line between prevention and cure; moreover the name given to the newly-created service was the 'sanitary department', the term 'sanitary' indicating the environment rather than the person. The officer in charge was known as the sanitary commissioner, on the analogy of the divisional or financial or excise commissioner.

At the time of the fission the parent department had its hands full with the ever increasing demand for medical relief and the new department relieved it of environmental hygiene, a subject which was then much more backward even than it is now. So long as the sanitary department kept to environmental hygiene there was little or no overlapping, more than ample scope existing for the energies of both services, except in time of epidemics when close co-operation was called for and readily given by both sides.

Later, the name sanitary commissioner was changed to director of public health, an appellation which, welcomed at the time, has had some unfortunate results in that it led many lay and even medical men to the erroneous belief that the medical department was not an integral part of the health services of the country or closely concerned with the public health. Nothing of course could be further from the truth, or more damaging to the efficiency of a state medical

department itself or to its relations with the public. One of the most important sections of the English Ministry of Health is that dealing with hospitals and the term 'public health' in England and in every other country that I know is interpreted to include hospitals and all other forms of medical relief.

Similarly, with the term 'health services'. The Political and Economic Planning Committee in their classic report on the British Health Services say: 'One of the first difficulties which arose was to find a satisfactory answer to the question—What are the health services? To take a narrow definition would have been to perpetuate the common mistake of using "health services" as a synonym for "sickness services"'. On the other hand, the subject would be expanded to an unmanageable extent if we were to follow to its logical end the view that health services cover all human activities which promote or might be used to promote health, including for example labour management, the design and pricing of food and clothing, housing and its location in relation to work and play, and the methods of using leisure. We have tried to strike a balance between these two views, on the one hand examining the importance of improving the services which deal with actual cases of ill health, and on the other emphasizing the need for a progressive widening of the idea of health services to bring in and co-ordinate many activities at present carried on without relation to, or actually in opposition to, the needs of national health'.

In England and elsewhere we have a unified system of control of the medical health services, in most provinces of India we have arbitrarily split the service and to some extent the profession into two sections. In England we have a medical officer of health, in India a medical officer and a health officer.

In a number of provinces people are beginning to ask why there are two medical services dealing with the one subject of health, what their separate functions and limitations are, what logical basis exists for these, why the system in India differs from that in other countries, and particularly why we have a unified system in some provinces and separate departments in others? These questions are not easy to reply to. The answer I usually give is that so long as co-operation is close and cordial the separate system works well but that, if co-operation fails and overlapping of function and duplication of staff appear, the remedy is unification of control.

There are many branches of public health work—and I use the term in its correct wide sense—in which the need for close co-operation between what I might call the clinical and the field staff is obvious. Examples are school medical work, tuberculosis, and leprosy. Perhaps still more striking is the subject which has inspired the formation of the Delhi Maternity Services Co-ordination Committee.

At its last meeting the Central Advisory Board of Health—itsself a body designed to promote co-operation—passed this resolution—

'Co-ordination between the medical and public health departments is perhaps more vital in the field of maternity and child welfare than in any other sphere of medical and public health work'.

It is sometimes argued that child-bearing is a normal physiological process of the body, automatic, self-regulating and entirely remote from disease. Ideally this may be so, but without the doctor and the nurse the process is associated with a maternal mortality in the neighbourhood of 25 per 1,000, and an infantile mortality which in India may be as high as 35 per cent.

Each stage pre-natal, natal and post-natal may with luck be safely negotiated without the aid of doctor or nurse, but it is a proved fact that that mother stands the best chance of safe delivery and a healthy child who obtains and follows expert medical advice throughout. Much responsibility can and in most cases must be devolved upon health visitors and midwives, but our efforts should be directed towards securing the minimum necessary examination and supervision by a qualified doctor in every case. A tendency, of

which I have seen evidence in this country, to short-circuit the doctor and rely entirely upon the judgment and skill of a health visitor or midwife requires to be countered and both the doctor on the one hand and the health visitor or midwife on the other should realize that each is complementary and therefore helpful to the other.

I have seen maternity and child-welfare centres located within hospital compounds and others a mile or more away. I don't think this is a matter on which a rule can be made; much will depend upon local circumstances. What is important is that no centre should try to work independently of a practising doctor and that no such doctor should think he can efficiently do his share of the work without attending regularly at the centre.

Pre-natal and post-natal clinics should be held by the doctor on regular days at the centre itself, cases requiring treatment at the hospital being given attendance or admission cards, and whenever possible being taken there by the health visitor. This I regard as important since it is just as desirable for the health visitor to attend and have a recognized status at the hospital as for the doctor to attend and have his recognized status at the centre.

The weak link in the chain at present is the connection between centre and hospital. It is here that misunderstandings occur and patients get discouraged and lost.

Where several centres are linked with one hospital definite arrangements require to be made as to the day or days in the week for sending patients for special examination or admission. Any inco-ordination here means delay and disappointment to the patients.

No one I think will question the desirability of having a qualified doctor booked and available on call at every birth, yet I imagine this is far from being realized in Delhi. I shall be interested to hear the views of those with local knowledge on the position in regard to this. The private practitioner must not be forgotten. There is perhaps a danger that in the natural desire to complete the official service the rôle of the private practitioner may be overlooked. Clearly if the medical profession are not to see obstetrics pass from their hands to the midwives it is essential that they undertake to attend cases of child birth, not only in those hospitals and maternity homes to which they have access but also in the houses of the people, and much of this work among the poorer classes must of necessity be free or subsidized.

If the centre is dependent upon the hospital, the hospital also needs to rely on the centre. In the case of patients coming direct to hospital, the doctor, if he knows and appreciates the help the centre can give, will be only too ready to avail himself of it and to put his patient in immediate touch with the nearest centre. It is remarkable however how little practising medical men, both official and non-official, know of the activities of health centres.

I have been impressed by the abuse of free hospital facilities on the part of those able to pay, that is occurring in various parts of India. In a country where medical relief is in any case grossly inadequate medical treatment given free at public hospitals and dispensaries to those able to pay, pauperizes the public, pauperizes the medical profession and accommodates the rich at the expense of the poor. In maternity and child-welfare work, as in other branches of our medical activities, it is necessary to guard against this abuse which is an encroachment upon the domain of the registered medical practitioner that, if permitted to develop, will lead to a lack of co-operation between the official and non-official members of our profession.

In regard to child-welfare work I feel that an equal or even closer association between hospital and centre, doctor and health visitor is called for. Each is an essential partner in the work and each must contribute his or her share for the benefit of all. Only in this way can misunderstanding and mistrust be removed from patients and staff alike and replaced by a genuine spirit of co-operation.

For the working out of the details of a provincial scheme of co-operation in maternity and child welfare a small *ad hoc* committee may be of value which should also meet periodically to consider the progress made and difficulties encountered.

Other points occur to me, but as I have already taken up so much time I shall only mention them briefly.

There is the use of centre *dais* for private cases, a question regarding which there are likely to be two views based on the danger of neglecting the indigent on the one hand and that of being exploited by the well-to-do classes on the other.

There is the question of how far centres should participate in medical treatment which is the same question of co-operation again, and lastly the important matter of utilizing the centres and their valuable contacts with the people in the training of medical students and nurses.

On all these points frank discussion to elicit the different points of view will be of value.

I am a fervent advocate of close co-operation in the medical health services of the country and between these and the great body of private practitioners. I was not always so ardent an advocate of co-ordination but experience gained in my service which has been both of curative and preventive work and in both the individual and community spheres of public health have I think given me a measure of binocular vision, and the picture I see more and more clearly as time goes on is that of one medical department of health co-ordinating and applying all technical knowledge and skill to the common goal of the maintenance and improvement of the health of the people.

#### ANNOUNCEMENT OF THE FRANCIS AMORY SEPTENNIAL PRIZE OF THE AMERICAN ACADEMY OF ARTS AND SCIENCES UNDER THE WILL OF FRANCIS AMORY

In compliance with the provisions of the Will of the late Francis Amory, the American Academy of Arts and Sciences, as Trustee of a fund given by the testator, announces a prize to be known as 'The Francis Amory Septennial Prize' to be awarded for conspicuously meritorious work performed during the immediately preceding septennial period, 'through experiment, study or otherwise, in the treatment and cure of diseases and derangement of the human sexual generative organs in general, and more especially for the cure, prevention or relief of the retention of urine, cystitis, prostatitis, etc.' While the donor wished especially to reward the discovery of any new method of treatment, he expressly authorized that the prize might be given to any author who might have contributed any theoretical or practical treatise of extraordinary or exceptional value and merit on the anatomy of the said organs or the treatment of their diseases.

If there shall appear work of a quality to warrant it, the first award will be made in 1940. The total amount will exceed \$10,000 which may be divided at the discretion of the Academy among several nominees. While formal nominations are not expected and no essays or treatises in direct competition for the prize are desired, the Committee invites suggestions looking toward the wise performance of their duty. Communications on this subject should reach the Committee not later than 15th May, 1940, and should be addressed in care of the American Academy of Arts and Sciences, 28, Newbury Street, Boston, Mass., U. S. A. The members of the Committee on the Francis Amory Septennial Prize are: Dr. Roger I. Lee, Chairman; Dr. Walter B. Cannon, Dr. David Cheever, Prof. Leigh Hoadley, Dr. William C. Quinby, Dr. E. E. Tyzzer and Dr. Soma Weiss, Secretary.

#### HEAVY DEMAND FOR CHOLERA VACCINE

DURING the year 1938, the demand for cholera vaccine manufactured by the Central Research Institute, Kasauli, beat all the previous records since 1927. The

epidemic conditions were chiefly responsible for the demand which was very heavy during the months from April to August. To cope with it, the staff at the institute had to work even on Sundays and other holidays. The Punjab and North-West Frontier Province and the contiguous Indian States and the Army were the main clients. The supplies also went to Afghanistan and Egypt.

The total issues of the prophylactic cholera vaccine approximated 2,000,000 c.cm. Of this 1,984,486 c.cm. were issued to indentors in India and 10,120 c.cm. to foreign countries in the Near East. The issues of the year 1938 were eight times as high as in the previous year.

The following figures show the issues over a period of six years:—

1933	..	462,002 c.c.	1936	..	731,700 c.c.
1934	..	601,590 c.c.	1937	..	241,458 c.c.
1935	..	1,836,820 c.c.	1938	..	1,994,606 c.c.

The manufacture of vaccines and sera continued on a large scale; and issues were heavy during the year. Prophylactic cholera vaccine and TAB vaccine were manufactured on the largest scale. The preparation and issue of anti-venom serum continued as in the previous year, with the difference that it also captured other markets such as Portuguese India and the Philippine Islands, in addition to the previous ones—Burma, Ceylon and Iran.

The Army in India remains one of the best buyers of the sera and vaccines of the Institute.

#### GONADOTROPIC AND LACTOGENIC HORMONES. INTERNATIONAL STANDARDS. DISTRIBUTION BY THE BIOCHEMICAL STANDARDIZATION LABORATORY

INTERNATIONAL standards for (a) the gonadotropic substance of pregnant mares' serum and (b) the

lactogenic (crop-gland-stimulating) substance of the anterior lobe of the pituitary gland (prolactin, galactin, mammothrophin) are now available for distribution at the Biochemical Standardization Laboratory, Calcutta. They have been prepared in accordance with the recommendations of the Third International Conference on the Standardization of Hormones, held at Geneva in August 1938.

The Biochemical Standardization Laboratory, which has been appointed by the Government of India as a 'National Centre' for the distribution of standard preparations of biological products, holds these standards on behalf of the League of Nations and sends them on request free of charge to any *bona-fide* research institution or commercial organization. The laboratory also gives all relevant information regarding the standards to those who are interested in their use.

#### THE GRAND PRIORY IN THE BRITISH REALM OF THE VENERABLE ORDER OF THE HOSPITAL OF ST. JOHN OF JERUSALEM

THE King has been graciously pleased to sanction the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem.

##### As Officers (Brothers)

Colonel (now Major-General) Gordon Gray Jolly, C.I.E., I.M.S.

Colonel Reginald Stephen Townsend, I.M.S.

Lieutenant-Colonel Alured Charles Lowther O'Shee Bilderbeck, M.R.C.S., L.R.C.P., D.P.H., I.M.S.

##### As Serving Brother

Lieutenant-Colonel Jordan Constantine John, O.B.E., M.B., M.R.C.S., I.M.S.

## Current Topics

### General Therapy of Pneumonia

By ROGER I. LEE, M.D.

(Abstracted from the *Journal of the American Medical Association*, 7th October, 1939, p. 1411)

At this date, May 1939, it is certainly premature to discard all other therapeutic devices and measures in pneumonia, and in all likelihood it will always be foolhardy to treat the disease pneumonia or any one of its symptoms exclusively and to ignore the patient. In truth the patient is the container of the disease. He then becomes the battleground of what formerly nearly always was and even now often is a titanic struggle. As the opposing forces line up and get into action and as the battle begins and goes on, the unfortunate patient or container of this devilish battleground is badly shaken and racked. Furthermore, during this turmoil the patient has functional obligations, including the transport of oxygen, serum and drugs to carry on. Moreover, according to our present beliefs the patient himself must actively participate in the battle against the invading enemy if cure is to result, no matter how specific drugs and serums seem.

Essentially the general management of a case of pneumonia consists in the conservation of strength. Rest and quiet are the prime considerations. There should be no delay in putting the patient, and that includes the suspects, to bed. Within the first twenty-four hours a patient may probably be moved without undue increase of risk in an ambulance (not an automobile) to a hospital, provided the distance is not over a few miles and provided the bed to bed journey

is accomplished with the smoothest possible arrangements. However, any move does actually increase the risk somewhat and after forty-eight hours of the disease the increase in risk to the patient is considerable. Therein often is required a wise balancing of benefits and hazards with the prejudice toward non-transportation after forty-eight hours.

In the home the so-called hospital regimen must be established, including a hospital bed and continuous nursing. By rest I mean the elimination of any unnecessary physical activity. The patient should not feed himself or give himself a drink. He should not turn over by himself. By quiet I mean the elimination of any unnecessary outside disturbance to the patient. This obviously includes visitors and also includes any unnecessary medical manipulations and examinations. Blood counts, blood cultures, physical examinations and x-ray examinations must be carefully organized in advance and carried out with precision and dispatch. Likewise the somewhat elaborate and technical procedures as intravenous serum therapy or intravenous fluid therapy or subcutaneous medication or fluid administration should be prepared as far as possible outside the room.

Probably next in importance is the supply of an adequate amount of fluid to the patient. On this subject there is a wide diversity of opinion. My own view is that the intake should suffice to keep the urinary output in the neighbourhood of 50 ounces (3 pints, or 1,500 c.c.). Less than this I regard as insufficient and much more than this as creating unnecessary work for the heart, circulation and kidneys. Some patients who sweat a good deal may have difficulty in getting in an adequate amount of fluid.



Other patients may have marked gastric disturbances in the early days of the disease. Perhaps a majority of patients who take sulphapyridine have gastric symptoms to a greater or less degree. Some of these patients will require fluid by some other route, although skilful nursing with a shrewd selection of fluid, e.g., the use of very weak, rather hot plain tea, and the avoidance of egg-nogs and of excessive fruit juices will diminish the number of patients who must be disturbed either by intravenous or by subcutaneous fluids. If there is vomiting and acidosis one may lean toward intravenous saline solution with dextrose, but my personal preference based on physiological grounds is for the subcutaneous route. The desirability of avoiding intestinal disturbance, either distention or diarrhoea, both of which are well-known bugaboos in pneumonia, usually decides against using the intestinal route for fluid.

In the average case of pneumonia in the acute stage, little attention need be paid to the caloric requirements. It is imperative to get in fluid and highly desirable to avoid distention or diarrhoea. Hence a low residue diet without much milk meets the requirements. Obviously food requiring chewing should be avoided, but minced chicken, mashed potato, soft toast, soft cereals, eggs, ice cream and apple sauce indicate the range of possibilities. With distention milk may be further reduced and cream added. Usually a mild vegetable laxative is given each night and an enema if necessary every other day.

The evidence is clear and strong that sodium chloride is diminished during pneumonia, through perspiration and in the pulmonary exudate. Therefore the salt in the diet is increased and frequently, if capsules are well tolerated, salt is so given in 5 or 10 grain (0.3 or 0.65 gm.) capsules up to 60 grains (4 gm.) a day.

While there is some evidence that ascorbic acid and probably some of the other vitamins are diminished in pneumonia, at this time and for this discussion it seems better to consider vitamin and iron therapy in the management of the convalescence and not of the disease.

Over the years the old saying has been repeated 'The disease is in the lungs but the danger is in the heart'. Translated into the terminology of to-day and without attempting a precise explanation of the complicated pathologic physiology, one may say simply that the danger lies in circulatory failure. After a very thorough trial the evidence is definitely against the value of routine digitalis therapy in pneumonia. In a previously undamaged heart and circulation, digitalis and its group are but rarely indicated. The indications for the exhibition of digitalis are the usual indications of an incompetent heart. The heart is seemingly stimulated early in the disease by the circulating toxins or the fever or both. Later in the disease those patients who seem likely candidates for cardiac incompetence from previous cardiac damage, hypertension or old age may be benefited by digitalis. A not uncommon cardiac symptom in patients beyond middle age and rarely before is the occurrence of a tachycardia, paroxysmal in type, of the nature of flutter or fibrillation. Such attacks usually cease spontaneously, but quinidine or digitalis or both are ordinarily indicated.

There may be, of course, in pneumonia a wide variety of incidental symptoms. Many patients have a previous familiarity with various members of the salicylate group. If sweating is not greatly increased and if the stomach is not disturbed, some comfort, ease of headache and of general malaise and diminution of fever may be attained by the moderate use of the salicylate group. The pleuritic pain, usually early, may be distressing. A swathe is better than drugs. The salicylates may of course be tried. The exhibition of large doses of opiates has been regarded as contra-indicated in pneumonia and with a good deal of supporting physiological evidence. On the other hand the desideratum of rest is so important that I feel no hesitation in using frequent small doses of morphine subcutaneously. By small doses I mean as small as

1/32 or 1/16 grain (0.002 or 0.004 gm.). This is also very useful in combating restlessness. The oral administration of morphine, codeine and opium has the objection of being decidedly constipating.

Fortunate indeed is the patient with pneumonia whose restlessness is controlled by one-fourth grain (0.016 gm.) of phenobarbital a few times a day and who sleeps soundly with phenobarbital or pentobarbital or some similar drug. I myself am reluctant to use any further medications than those I have mentioned, but there are always exceptions.

As far as I know the only usefulness of alcohol is, if in small and nondisturbing doses, it creates a beneficial mild euphoria. Alcohol does not seem to me to have any important place in pneumonia therapy.

I mention diathermy and pulmonary collapse therapy merely to confess inadequate experience with these and similar procedures and to give my impression that at this time they do not seem to occupy a place in the management of pneumonia.

Time does not permit a discussion of the various complications and sequelae of pneumonia. Furthermore until further experience and data have been gained with the newer and more effective therapeutic agents, serums and chemicals, alone or in combination, physicians are in no position to discuss the management of these conditions intelligently.

The general treatment of the pneumonia patient as I have outlined it seems highly innocuous in contrast to the era in which bleeding, purging and puking were almost routine. Likewise physicians have given up cupping, counter-irritation and poultices. They no longer subject their patients (and the nurses) to the icy blasts of winter. However there may be merit in the air-conditioned room in summer and perhaps in a room where the temperature can be controlled.

Even if slush baths are not used for reduction of temperature, certain forms of bathing which have a sedative effect are regarded highly. That and the judicious employment of rubbing or of massage are accepted as a part of good nursing care.

In effect, an attempt is made to manage the patient so as to conserve his strength, so that he may be fortified against the devastating tumult of the battle within him and that he may contribute what he can to the suppression of the enemy pneumonia. Pneumonia is always to be regarded as one of the doctor's most common major emergencies. Loss of time may mean loss of life. During the few days of emergency, no detail is trifling. And while the glory of a victorious battle will go to the big guns of chemotherapy, serum therapy and oxygen therapy, this battle, like other battles, is often actually won by the nonspectacular infantry, in this case, the general care of the patient.

### Painful Eyes

By R. F. MORE, F.R.C.S.

(From the *Medical Press and Circular*, Vol. CCII, 11th October, 1939, p. 304)

IN dealing with the question of painful eyes it will be convenient to consider them in two classes.

In one group we shall have cases where there is some disease or lesion of the eye itself which is responsible for the pain, such as iritis, and in the other will be included those numerous cases variously described by the patient as discomfort, aching, smarting, pain or even severe pain in eyes which themselves are entirely free of any discoverable abnormality.

I have often thought it would be instructive if one had a measure of pain in the way that we have of body temperature, for no one will doubt that what one person will refer to as discomfort another will describe as pain, or perhaps even excruciating pain.

Pain in the eye can be very severe, especially in cases where the intraocular tension is raised, and I think it is a feature of eye pain that if it is at all severe it is persistent, and the patient is not accorded those periods of remission or temporary relief which are granted to most other sufferers from pains in other parts.



It may at the outset be accepted as an axiom that if pain is complained of in an eye which is entirely free of redness, such pain is not an indication of organic disease, and to this I know of one only seeming exception, to which I shall refer.

Let us first say something of pain referred to the eye but which has some distant cause. I suppose it is true to say that the eye is the most sensitive organ in the body and consequently if an individual is out of sorts it is not surprising to find that the eye acts as a sort of indicator of the general ill or well being. Folk who, without being ill, are in poor condition, will complain that on awakening in the morning their eyes smart and feel dry, and it is some time before they are made comfortable by blinking. I think of this as being due to their eyes having remained still during the night hours and so there has been a minimum of tears from the absence of eye movement.

A large number of patients who consult an ophthalmic surgeon do so because their eyes ache; they ache when reading or sewing perhaps, and in many instances the symptoms are caused by errors of refraction, and some by muscle imbalance. There is no doubt that these two imperfections when uncorrected are responsible for a great deal of discomfort estimated in the consciousness of some as actual pain. But apart from any such errors one is often told that the eyes ache when motoring, or in cinema or theatre or when something is looked at fixedly for a short time, or indeed without any known reason. One finds it difficult to allocate a cause of these. For motoring I have thought perhaps the constant attention on the road and the constant movement of the eyes might explain it, that in fact it had a muscular origin. For cinemas and the theatre perhaps the flicker of the pictures and the unusual and rapid change of scene of the latter, and perhaps the lack of ventilation in both.

There is a painful condition, which affects one eye only, which is usually described as a burning feeling. I have heard it said it was as if a drop of mustard oil had been dropped into the eye; it continues for years. I have watched one such case for more than twenty years. The pain during that time has fluctuated but has disappeared for short periods only, and has been sufficient considerably to curtail the individual's reading capacity. The removal of teeth has not altered it and now at the end of more than twenty years the functions of the eye are unimpaired and it is free from all signs of disease. I have wondered whether the sinuses could be completely exonerated, but have been reduced to thinking of it as neuralgia.

The involvement of the trigeminal nerve in a neoplasm or in inflammation may cause pain referred to the eye, and later neuropathic keratitis may develop.

May we now give attention to those cases where the pain is clearly due to a pathological change in the eye itself, and in distinction to the former group, the pain in this group is accompanied by a varying degree of redness of the eye, and usually by ptosis and lachrymation.

The characteristic description of the pain of conjunctival or corneal disease is of a gritty feeling, as if the eye was filled with sand, or as if something were in it. It may be that a foreign body is present either in the cornea or under the lid, the latter is much the more uncomfortable for with every movement it scrapes over the highly sensitive cornea. A corneal ulcer or abrasion may be present. Iritis is a cause of what may properly be called severe pain in the eye, although there is a variety which is usually called 'quiet iritis', in which there seems to be no pain, and in which all the signs of acute disease are slight.

The pain of acute iritis is often compared with severe toothache. It is felt deep in the eye, along the side of the nose or in the malar bone.

The pain of cyclitis, interstitial keratitis, and scleritis is in general similar to that of iritis, but is less severe; that of scleritis is often worse at night.

In herpes zoster of the ophthalmic division of the fifth nerve the eye itself usually becomes involved if the nasal branch of the nerve is affected; the cornea,

iris and ciliary body are involved and the eye remains inflamed and painful for many months.

Particular mention should be made of the pain of an attack of acute glaucoma for it is especially severe and indeed so severe as often to cause nausea or vomiting, and as a consequence of this it is no uncommon thing to find the eye condition almost ignored and a diagnosis of some acute abdominal condition made. The resulting delay in the treatment of the eye has many times led to a quite unnecessary and irreparable blindness.

**Retrolbulbar neuritis.**—By this title is embraced any involvement of the optic nerve posterior to the globe, and whilst the term would seem necessarily to indicate an inflammation of the nerve, it is generally used in a comprehensive way to include any cause which affects the nerve, though its nature may not be clearly inflammatory.

One of the special features of retrolbulbar neuritis is a deep-seated pain which is made worse by moving the eye or on pressing it backwards into the orbit. It is the outstanding example of organic disease in which no sign of inflammation of the eye is present. It is, however, an involvement of the nerve behind the globe rather than of the eye itself.

By a long way the most important cause of acute retrolbulbar neuritis is disseminated sclerosis, and indeed it may be said that acute retrolbulbar neuritis occurring in young adults up to middle age is disseminated sclerosis, if diabetes and obvious exogenous poisons, e.g. methyl alcohol, can be excluded, and this is true even though at the time no other discoverable evidence of the nervous disease is present and may not develop, as I have seen, for twenty or more years.

Inflammation of the sphenoidal sinus is believed by some to be a source of retrolbulbar neuritis and it has been stated that it is this cause that produces pain on movement of the eyes, and that the pain on movement is indeed characteristic of this cause.

That the retrolbulbar neuritis of disseminated sclerosis causes pain on movement I can be sure, and I would go further and say that whilst the close relationship of the optic canal to the sphenoidal sinuses would make it seem likely that inflammation of that sinus might spread to the nerve and cause retrolbulbar neuritis, yet in spite of repeated investigations carried out in conjunction with skilled rhinologists, I have never seen a case in which I was in any way satisfied that sphenoidal sinusitis had produced retrolbulbar neuritis. In this connection it is important to have the fact in mind that the recovery of sight in the retrolbulbar neuritis of disseminated sclerosis is frequently as rapid as the failure, indeed a large measure of recovery may occur in forty-eight hours. It is clear that unless this is remembered a dramatic restoration of vision may be claimed as a cure for some form of treatment, operative or otherwise, which happens to have been instituted at just the right moment.

One is sometimes asked whether pain in the eye is due to rheumatism, the patient volunteering that he is a rheumatic subject. In the absence of any cause that one has been able to discover, the temptation is present to shield one's ignorance and accept rheumatism as a possible cause, and in this one has at least the support of Jonathan Hutchinson. I can only say that it may be a cause, but where so large a proportion of individuals is ready to attribute certain indefinite pains in any part of the body to rheumatism, and so to believe themselves to be 'rheumatically', it would be extremely difficult to substantiate that pain in the eye was not due to the same uncertain cause.

Lastly may we consider what measures are available for relief of pain in the eye. I mean local applications; for the general relief of pain by narcotic drugs need not come within our scope.

With regard to the pain which accompanies corneal, and to a lesser degree conjunctival lesions, the application of a pad of wool bandaged on rather firmly is helpful by restricting the movements of the eye and so limiting the rubbing together of damaged surfaces,

and to carry this principle further it is more effective if both eyes are bandaged, for if one eye is left open it is sure to look about and so the other eye moves with it; if there is virulent infection with pus formation it is unwise to bandage it in this way. Some bland lubricant, such as parolein or castor oil, acts helpfully in the same way.

Immediate relief is obtained by means of cocaine, but it has so deleterious an effect upon the corneal epithelium that it should not be used for the purpose we have in mind. Besides, the relief it gives is of short duration.

In the treatment of corneal ulcers and recurrent corneal abrasions, whilst the application of pure carbolic acid causes smarting pain rising to a maximum in three to four hours, its after effects both as regards pain and permanent healing are so beneficial in a case of any severity that it is well worth reminding ourselves of its high value.

In intraocular inflammation such as iritis or cyclitis, and where the question of increase of tension does not arise, atropine is valuable; it is best used in the form of 1 per cent of the alkaloid in soft paraffin. It eliminates all the movements of the iris, and the contraction of the ciliary muscle, and besides breaks down or prevents the formation of adhesions of the iris to the lens.

Heat applied in various ways is soothing and generally beneficial. It may be applied in the form of hot bathing; the head is held over a bowl of hot boracic lotion in which several swabs of cotton-wool are placed. These are picked up on a wooden spoon or stick and held against the closed lids; when a swab begins to cool a fresh one is applied, the used one being dropped back into the hot lotion. The lotion is kept hot by the addition of boiling water as necessary.

Boracic fomentations are comfortable either by themselves or when alternated with dry heat.

Dry heat is best applied by means of an electric pad, which is kept in position with strapping or a bandage. A thin layer of wool or gauze is placed between the pad and the eye, and a thicker layer outside it in order to conserve the heat. The appliance can with benefit be kept on for many hours a day.

Leeches are really valuable, not only for the relief of pain, but for their beneficial effect in acute iritis, cyclitis, or acute or subacute glaucoma. Two or three are applied to the temple. A mixture of equal parts of camphor, thymol, chloral hydrate and chloroform may be gently rubbed on the temple, forehead, or over the mastoid, to give some measure of relief of pain; care must of course be taken that it does not go into the eye. Tincture of iodine may be painted on the temple and will at least do no harm. A blister, one inch square, applied to the temple will often help in the relief of pain.

### The Treatment of the Patient with Severe Burns

By R. D. McCLURE, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXIII, 11th November, 1939, p. 1808)

#### TREATMENT OF BURNS—HENRY FORD HOSPITAL METHOD

It is important to bear in mind the necessity of treating the patient as well as the wounds. Treatment naturally resolves itself into three phases: supportive measures, local treatment of the burned areas, and after-care.

*General supportive measures.*—These are largely directed toward the control of symptoms.

1. Pain and restlessness are combated by adequate and repeated sedation.

2. Oxygen therapy may be indicated in certain severe cases.

3. External heat is applied: hot water bottles and blankets if the burned area is limited; in extensive burns, the electrically heated cradle tent and super-heated room.

4. Restoration of fluid balance is undertaken. The aim of fluid administration should be to obtain a twenty-four hour urinary output of 1,500 c.c. Fluids are given by mouth if tolerated, by rectum, interstitially and intravenously. The continuous intravenous method is often indicated and may be imperative in cases of extensive burns involving the extremities. The solutions used are 5 per cent dextrose and physiologic solution of sodium chloride.

5. Blood plasma transfusions are done. Whole blood should be used only when blood concentration is normal, as indicated by repeated hæmoglobin or hæmatocrit determinations. When hæmoglobin values of more than 15.6 gm. are obtained, plasma transfusions should be given.

6. Laboratory investigations are made:

(a) Frequent hæmoglobin or hæmatocrit determinations should be made.

(b) The urine should be analyzed frequently, with determinations of the specific gravity and albumin content.

(c) Serum protein determination should be made immediately on admission.

When facilities are available, the following procedures should be done:

(d) Chloride estimations should be made at intervals so that depleted chlorides may be restored by intravenous administration of saline solution.

(e) Blood cultures may be taken.

(f) The nonprotein nitrogen should be determined.

(g) The icterus index should be ascertained as a means of recognizing toxic hepatitis or liver damage.

*Local treatment.*—1. Remove all clothing under as sterile conditions as possible and place the patient on sterile sheets in a warm room.

2. Take all precautions to avoid infection of the burned area. Treat it just as any other large wound. All dressings and applications must be done under aseptic conditions—masks, gloves and gowns must be worn by doctors and nurses.

3. Débridement should be minimal and should be limited to opening blisters and cutting away dead skin.

4. Tannic acid in a 5 per cent fresh solution is applied with an atomizer or power spray. This is a simple and effective way of tanning the burned area. This solution is sprayed on at frequent intervals until the burned area is thoroughly tanned. Ointments containing tannic acid plus an antiseptic are useful in small burns and for burns of the face and the perineum. The addition of antiseptics such as resorcinol or silver nitrate to the tannic acid with the idea of preventing infection has been employed with apparent success, but treating the burned area as a surgical open wound by taking steps to prevent the introduction of infecting organisms is an equally, if not more, effective measure.

*After-care.*—1. Cut away all dead skin and open collections of fluids under aseptic precautions and then again spray tannic acid on the bared areas.

2. As the heavy tanned crust forms, watch carefully for local signs of infection under the crust and liberate collections of pus. Occasionally the first clue to these collections is evidence of systemic reaction.

3. Prevent contracture deformities by the early use of extension apparatus.

4. Employ skin grafting early and freely.

5. Detect and treat secondary anaemia early. Blood transfusion is the best method of doing this in the late stages.

#### COMMENT

We have continued to advocate the use of tannic acid in the local treatment of the skin. Variations in the technique have been successful. Other eschar-forming chemicals, such as gentian violet and silver nitrate, have given satisfactory results. The advantages claimed are that the coagulum forms more quickly and is thinner and more pliable than that produced by tannic acid. Bettman has had excellent results with a combined tannic acid-silver nitrate treatment. He believes that the combination is superior to tannic acid alone, and his experience would tend to bear out this contention. He attributes the improvement to the

increased antiseptic qualities of the mixture and to the fact that the coagulum is produced without delay. We have found that the tannic acid may be conveniently applied to the medium of a water-soluble jelly to which has been added an antiseptic of the resorcinol group.

#### SUMMARY

The original theory that a toxin is formed in the burned area, from which it is absorbed and carried by the circulation throughout the body, with the production of systemic effects has not yet been settled. In spite of excellent results being obtained in many centres, the death rate in the United States seems to have reached a plateau far above that lower level which is possible with our present knowledge. Disagreements regarding the proper local treatment should not distract our attention from the more important problem—the treatment of a very sick patient who has a threatening toxæmia, alterations in the blood chemistry, a wound very susceptible to infection and pathologic changes in organs remote from the skin. The greatest good can, of course, come through preventing burns from occurring, and I believe that the family physician, through his teaching in the home, can accomplish more than any other agency in this respect.

### The Use of Colloidal Calomel Ointment in Dermatology

By T. CORNBLEET, M.D.

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and

M. H. EBERT, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXIII, 11th November, 1939, p. 1804)

MERCURY ointments in various forms have long been a standby for the dermatologist. First, metallic mercury ointments were employed, and in recent times the ammoniated mercury ointment has enjoyed tremendous vogue. In the last few years, calomel ointment has been used in the so-called clean inunction method in the treatment of syphilis.

Calomel ointment, first prepared in France during the last century, contained 10 per cent of calomel in petrolatum. The British used 20 per cent of calomel in lard. A 30 per cent ointment with white petrolatum was introduced into the National Formulary V (1926) under the name of Ointment of Mild Mercurous Chloride. In N. F. VI (1936) the base was changed to equal parts of white petrolatum and hydrous wool fat.

Dr. Lewis C. Britt, chemist of the Oregon State Board of Pharmacy, first pointed out that the N. F. VI ointment gave a narrower inhibitory ring in the agar plate test for antiseptics than did the N. F. V. ointment.

Mr. E. E. Vicher at the University of Illinois College of Pharmacy undertook the study of the ointment. He developed calomel in which the particles were very small, 0.5 micron or less in diameter. This calomel in aqueous suspension with gelatin was incorporated into the ointment base. The new calomel ointment produced an inhibitory ring from three to six times as broad as did the official calomel ointment.

The improved or 'colloidal' calomel ointment has been extensively investigated from the chemical, bactericidal, pharmacologic and toxicologic standpoints. It appears to be no more toxic and the N. F. ointment, which has never been considered as toxic for human beings in doses 1 drachm (4 gm.). It has a prophylactic value in syphilis at least equal to that of the N. F. VI ointment.

As it is not unreasonable to expect that a colloidal calomel application with its demonstrated efficiency as a superior bactericidal agent should find use in certain cutaneous disorders, this colloidal calomel ointment has been used in the dispensary of the dermatologic clinics

of the Cook County Hospital to a sufficient extent to justify a preliminary report.

#### USE IN IMPETIGO CONTAGIOSA

We have found its greatest therapeutic value to be in impetigo contagiosa. In about 130 cases of this infection colloidal calomel ointment has served as an extremely efficient remedy. The use of ammoniated mercury ointment has long been a standard agent in impetigo, but all experienced dermatologists attest the observation that for some reason this medicament is not as efficient as it was in the past. According to our observations, colloidal calomel ointment clears the eruption in an average of one-third to one-half the time required by ointments of ammoniated mercury. This is particularly gratifying since the colloidal calomel ointment is both cleanly and, so far as our experience goes, not toxic. In not more than three or four instances it has produced a slight irritation, but this was not great enough to necessitate its withdrawal. Its cleanliness is to be emphasized because it gains the patient's co-operation and makes it a favourite over other efficient agents, such as applications of gentian violet solution.

Colloidal calomel ointment was found useful in other superficial pyodermas in addition to impetigo. In ecthyma, the base of the lesion is so deep as to require removal of the overlying crust, whereupon the colloidal calomel ointment proves curative. In Bockhart's impetigo, which is a more superficial infection of the hair follicles than that in furunculosis, and in furunculosis itself, no benefit was obtained from the use of colloidal calomel ointment.

#### ERYTHEMATOUS DERMATITIS BEHIND EAR

There is a condition which produces a superficial erythematous dermatitis in the fold behind the ear which is diagnosed most often as seborrhoeic dermatitis and which some authorities think is due to a streptococic infection. This is particularly resistant to treatment and especially so in that form in which the disease process reaches around to the front of the ear. In several cases of this disorder, the use of colloidal calomel ointment has been of benefit. It has been more effective than any other agent we have used.

#### INFECTED LEG ULCERS

Three patients with leg ulcers which, by their appearance, were undoubtedly continued or aggravated by secondary pyogenic infection, received much benefit from applications of colloidal calomel ointment. With no other treatment than the usual advice to the patient to remain off his feet as much as possible, these ulcers healed. In a number of other instances of leg ulcers on a basis of poor circulation, these applications were of no benefit.

#### OTHER DERMATOSES

Several patients with early psoriasis were benefited by applications of colloidal calomel ointment. It must be emphasized that these early cases are as a rule easily improved by ammoniated mercury ointment and that improvement with the calomel ointment represents no great triumph. In older cases of psoriasis and in the inveterate ones, colloidal calomel ointment did not improve the lesions.

Since colloidal calomel ointment proved to be so efficient in some of the superficial infections, it was hoped that it might likewise be beneficial in the superficial fungous infections such as eczematoid ringworm. Unfortunately, colloidal calomel ointment did not influence these infections.

There is a relatively superficial, sharply defined, exudative, patchy dermatitis that occurs on the backs of the hands and forearms particularly, but which may appear elsewhere also, called infectious eczematoid dermatitis. This probably results from the secondary infection of an already irritated base. Several of these cases were improved by applications of colloidal calomel ointment. Two of them were irritated by this form of treatment, so that it had to be stopped.

A number of other dermatoses were treated with the colloidal calomel ointment more or less unsuccessfully. There is no benefit from its use in lichen planus, paronychia due to yeast infections, pityriasis rosea, tinea circinata, lupus erythematosus or lupus vulgaris.

#### SUMMARY

Colloidal calomel ointment in this study was found to be a clean, unusually effective agent in impetigo contagiosa and related superficial pyodermas. Seborrhœic eczema behind the ears, which is often quite resistant to treatment, was favourably influenced by applications of colloidal calomel ointment. It improved leg ulcers aggravated or continued by a secondary pyogenic infection; also some forms of seborrhœic eczema and early cases of psoriasis. In other dermatoses, colloidal calomel ointment either was without benefit or proved to be irritating.

### Easton's Syrup: An Examination of the Changes occurring during Storage

By W. T. WING

(Abstracted from the *Quarterly Journal of Pharmacy and Pharmacology*, Vol. XII, July to September, 1939, p. 563)

EASTON'S syrup prepared according to the formula of the *British Pharmacopœia* 1932 is unsatisfactory, because it (i) rapidly develops a colour, first pink, later darkening to brown, (ii) deposits a white precipitate, and (iii) supports the growth of the moulds. The writer studied the changes and chemical reaction involved by storing the medicine in bottles loosely plugged with cotton-wool to allow exposure to air, and at normal temperatures under conditions most favourable to the development of changes. As a result of this observation he maintains that (i) there is no development of colour in the absence of iron, (ii) part of the colour, in which sucrose plays some part, is due to oxidation of constituents other than the alkaloids, (iii) the main colour is due to an oxidation reaction involving both the ferrous phosphate and quinine, and (iv) sucrose and glycerin retard the latter reaction. It is known that, owing to oxidation by air, ferrous iron is oxidized to the ferric state. The writer's opinion is that the ferric phosphate so formed in the syrup is still further oxidized, the presence of sucrose facilitating such a reaction, to any oxy-salt, producing a brown colour. The nature of reaction is supposed to be that in the presence of ferrous phosphate as a catalyst, quinine is oxidized by oxygen of air to quinone, quitenine, then quiteninone. Meanwhile ferrous phosphate is slowly oxidized to ferric phosphate and the ferric iron combines with these oxidation products, most probably with quiteninone which contains an acid group, forming coloured compounds. The earlier product or products of oxidation give a pink colour, where the later compounds give the brown colour. Glycerine tends to stop the reaction at the first stage where the pink compound is formed, whereas sucrose allows the reactions to go to completion, although both substances retard the rate of reaction. In the absence of iron no oxidation products of quinine form and therefore there is no intensification of colour.

The precipitate consists of amorphous ferric phosphate and acid quinine phosphate (one molecule of quinine united with one molecule of phosphoric and sulphuric acids), the latter of which are crystals (i.e., quinine sulphate phosphate) and may be absent on account of the solvent action of glycerine where this is present in the syrup.

The studies have also been made in this investigation regarding the factors affecting the development of colour and precipitation, viz, temperature, light, oxygen, modification of the vehicle, addition of organic and inorganic acids, and it has been summarized that

- (i) glycerine is advantageous in reducing the degree of coloration,

- (ii) the problem of precipitation is best approached by the use of acids which readily form soluble salts,
- (iii) hypophosphorous acid, a reducing agent although it retards precipitation, causes a greater development of colour,
- (iv) hydrochloric acid is most satisfactory in preventing coloration and precipitation, and
- (v) owing to the fact that moulds will grow in the present official syrup, an increase in the syrup or glycerine content is indicated.

The paper has also suggested an improved formula and its method of preparation,

Iron	..	8.6 gm.
Phosphoric acid	..	35.0 c.cm.
Strychnine hydrochloride	..	0.3 gm.
Quinine hydrochloride	..	13.3 gm.
Dilute hydrochloric acid	..	50.0 c.cm.
Syrup	..	660.0 c.c.
Glycerine	..	140.0 c.cm.
Distilled water	..	to 1,000 c.cm.

Phosphoric acid is dissolved in 70 c.cm. of distilled water in a suitable container. Iron is added to this and dissolved by heat on a water bath, and to this a solution of strychnine and quinine hydrochlorides in dilute hydrochloric acid (50 c.cm.) is added. The whole is filtered into the syrup and glycerine, previously mixed, and sufficient distilled water is next added through the filter to produce the required volume. This is the acid solution of the alkaloids and ferrous phosphate. The acid solution crystallizes on long standing and cooling. Glycerine, 140 c.cm., dissolves without the application of heat and crystals formed in 200 c.cm. of this acid solution only by shaking occasionally, showing that quinine hydrochloride phosphate is readily soluble in this solution. The colour and precipitation will be inevitable to a certain degree but they are not formed to any great extent with the improved formula. (Abstracted by M. L. C.).

### Surgery of the Common Bile-duct (Bradshaw lecture for 1939)

By SIR JAMES WALTON, K.C.V.O., M.S. (Lond.),  
F.R.C.S., F.A.C.S.

(Abstracted from the *Lancet*, Vol. II, 16th December, 1939, p. 1253)

THE biliary tract is subject to many anatomical variations, several of which are of great surgical importance. The cystic artery may lie below or in front of the cystic duct or curve in front of the hepatic duct and, if accidentally cut, cause severe hæmorrhage, in the controlling of which the common bile-duct or the hepatic duct may be tied (figure 1a). The main hepatic artery or its right branch may loop up behind the gall-bladder (figure 1b) and be divided in mistake for the cystic artery, causing necrosis of the liver. Very rarely the cystic duct is absent, the hepatic duct or ducts opening into one side of the gall-bladder and the common duct emerging on the other (figure 1c). Much more commonly the cystic duct is unusually long and even opens into the ampulla (figure 1d). If this is not recognized, stones in the common duct may easily be overlooked, and after cholecystectomy a portion of cystic duct may be left, which may dilate into a pouch, containing stones, almost as large as the original gall-bladder.

It is often in the seemingly easy case that danger arises, for a thin patient with a low, mobile and easily everted liver often has mobile ducts, so that traction applied to Hartmann's pouch draws out a loop of the common duct (figure 1e), which is mistaken for the cystic duct and divided. This danger is greatly increased if the resection of the gall-bladder is begun at the fundus, when the traction is greater and the deep field obscured by blood. The cystic duct (figure 1f) or a dilated Hartmann's pouch (figure 1g) may be so adherent to the common duct that the latter may be

mistaken for the cystic duct and divided. So common are these variations that it should be an invariable rule that no structure in this region should be divided until all three ducts and the cystic artery have been identified (figure 3b).

Sometimes the duct has not been completely divided, but the injury had led to a stricture and incomplete obstruction. All such strictures of the common duct are not, however, due to injury at a previous operation. It is often stated that a stone which has long been impacted in the common duct, and which may occasionally perforate it, may cause ulceration which in its later healing may stenose and obstruct the duct. In my experience this has been very rare. In my own series there were 20 cases of division, six traumatic strictures and five inflammatory strictures.

#### REPAIR OF LESIONS

These lesions, if recognized at the time, can generally be rectified by immediate end-to-end suture; but if they are unrecognized one of two conditions will follow. If the upper end of the duct is open, the bile escapes and does not pass into the intestine. Such patients may remain in fair health for a considerable time, and an operation for repair will usually be performed before their condition has seriously deteriorated. If, on the other hand, the duct has been ligatured, the patient rapidly becomes profoundly jaundiced, with complete absence of bile in the stools. Her health rapidly deteriorates, owing to back pressure on the liver, and at times the secretion of bile pigment may cease entirely, so that the distended duct is filled with a fluid like thin mucus, the so-called white bile. Any operation on such a patient is a serious risk. The most hopeless examples are those in which the common duct has been divided below in mistake for the cystic duct, and, as the gall-bladder is drawn out by traction, the two hepatic ducts are again divided high up in the hilum of the liver, into which they retract, so that at the second operation no trace of the duct can be found.

When there is a fistula or obstruction, the lower end of the duct is, as a rule, indiscernible, and the upper end of the duct has to be united with the duodenum; for the gall-bladder has generally been removed, and a cholecystoduodenostomy is therefore impossible. If the cut end of the duct can be easily approximated to the duodenum, Mayo's direct implantation often suffices; but it is difficult to make a valvular opening,

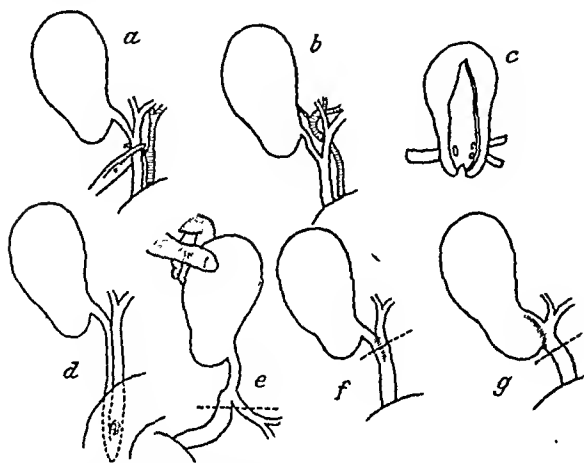


Fig. 1.—Anomalies possibly leading to lesions of the bile-ducts; (a) cystic artery lying below cystic duct has been accidentally cut, and in controlling the hæmorrhage the common bile-duct is accidentally clamped; (b) loop of hepatic artery occupying normal position of cystic artery; (c) congenital absence of cystic duct; (d) long cystic duct opening into ampulla; (e) mobile loop of common duct drawn up by traction on gall-bladder; (f) cystic duct adherent to hepatic duct; (g) Hartmann's pouch adherent to common bile-duct.

and there is a risk of ascending infection. A fistulous tract may be carefully separated from the abdominal wall, and its lower end may be implanted into the duodenum, but this does not give a valvular opening, and the greater part of the new duct, not being lined by epithelium, is liable to cicatrize and stenose, leading to obstruction. When direct anastomosis is impossible, the Sullivan method of inserting a tube between the cut end of the duct and an opening in the duodenum and wrapping the tube in omentum can be used. Here again the internal fistula left between duct and duodenum is lined by omentum only and likely to stenose. To overcome these dangers of subsequent stenosis and ascending cholangitis in the absence of a valvular opening into the duodenum, I devised an operation (figure 2) whereby a new duct was made from a flap of duodenal wall, which was sutured round the tube inserted by the Sullivan method. This ensured an epithelial lining for at least three-quarters of the circumference of the duct and allowed a valvular opening. If the liver has suffered badly from back pressure, much improvement may follow a slow decompression. The duct is opened, a long tube inserted and fixed, the wound closed, and the liver slowly decompressed. At a second operation performed about two weeks later the tube is cut off about 3 inches below the duct, an opening and flap made in the anterior wall of the duodenum, and the new duct reconstructed in the usual way. In the almost hopeless cases in which no trace of the upper end of the duct can be found an incision may be made into the liver substance, and the resulting biliary fistula may be united to the duodenum.

#### CONGENITAL DIVERTICULUM

A congenital diverticulum of the common bile-duct consists of a very rare dilatation extending from the duodenum to the cystic duct or sometimes to the hepatic ducts (figure 3a). Its contents may amount to

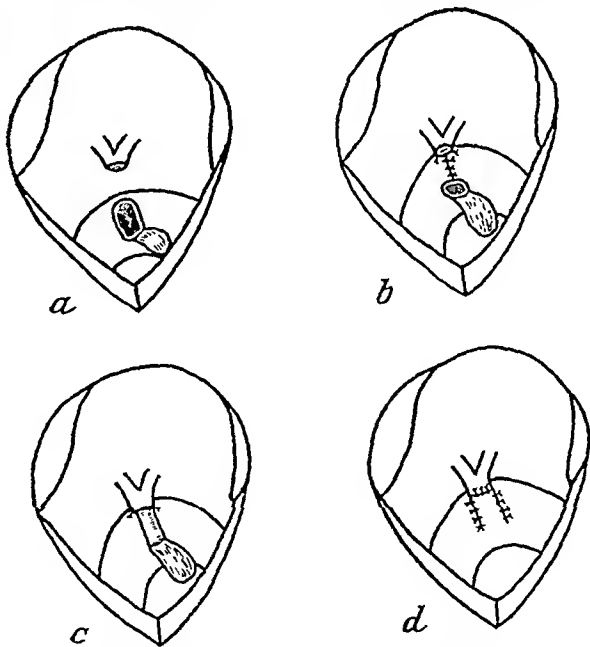


Fig. 2.—Reconstruction of common bile-duct; (a) opening made in duodenum and flap turned back; (b) suture of stump of common bile-duct to duodenum and closure of upper part of opening in duodenum with sutures; (c) insertion of tube to connect stump of common bile-duct with opening in duodenum; (d) suture of duodenal flap round tube.

several pints, suggesting an ovarian cyst or even a pregnancy. The most constant symptom is attacks of severe colicky pain, often associated with jaundice. The diverticulum has been known to rupture, the



symptoms then resembling those of a perforated peptic ulcer. Not only is the condition often overlooked on clinical examination, but also it may be missed at operation. The reason is probably that the gall-bladder is generally not dilated, and the diverticulum may be covered by membranous sheets. It cannot be too strongly emphasized that, if a patient has symptoms

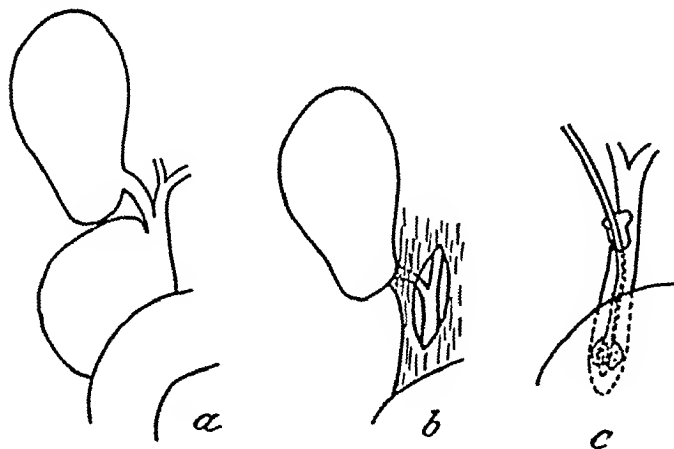


Fig. 3.—(a) Congenital diverticulum of common bile-duct; (b) exposure of all three ducts; (c) removal of stone through stump of cystic duct.

suggesting gall-stones, the common duct must always be examined. If this rule is followed, the diverticulum cannot be overlooked. If left, the condition appears to be always progressive and ultimately fatal owing to back pressure on the liver. A choledochoduodenostomy should always be performed.

#### IMPACTED GALL-STONE

Of the acquired lesions of the common duct the commonest is the impaction of a gall-stone.

*Symptoms.*—As a general rule, when a stone passes down the duct it causes attacks of severe colic, shortly followed by evidence of interruption in the flow of bile: white stools, dark urine and jaundiced skin and conjunctivæ. The stone may then pass and the whole attack be over; but, even if the stone does not pass, the spasm of the duct may abate, the bile pass again, and a false sense of security arise. Soon, however, the attacks are repeated, and, although the pain tends to become steadily less, the jaundice becomes more persistent, although the characteristic form a jaundice in this type of obstruction is variable or perhaps even definitely intermittent. The skin and conjunctivæ tend to remain bright orange, unlike the grey-green appearance in the late stages of the jaundice of a complete obstruction. Although the obstruction is incomplete, the duct becomes dilated and perhaps infected, and the liver rapidly suffers from back pressure. Although the ducts dilate, the gall-bladder is rarely distended from impaction of a stone in the common duct, probably because it is fibrosed from previous attacks of cholecystitis.

*Jaundice.*—It is usually taught that an operation in the presence of jaundice is a serious proceeding, and that it is better to wait until the jaundice has disappeared. This is entirely contrary to my experience. The risk in my cases has always been due to the back pressure on the liver, and, although the jaundice may vary, the damage from the back pressure steadily progresses as long as the obstruction remains. The danger of hæmorrhage in the presence of jaundice has always seemed to me an academic myth, and I have found little or no value in preliminary calcium therapy. The patient may be watched for a few days to see if the stone will pass, but, generally speaking, the presence of jaundice is an urgent indication for operation. For this reason the diagnosis of obstructive jaundice from that due to a toxic or infective hepatitis is extremely important.

The differential diagnosis is best made from the clinical history and by physical examination. In my cases the van den Bergh test has been of very little help. Jaundice due to hepatitis usually has an insidious onset with no pain. There is often a slight pyrexia during the first few days, or, if the jaundice is of toxic origin, there is evidence of gastro-intestinal disturbance preceding the jaundice. In the infective cases several persons living in the same house may have been affected, and there is no past history. The jaundice may be complete or incomplete, and in the early stages the liver is usually enlarged and often tender. In some cases of gall-stone obstruction, however, colic is absent; but there is usually a past history of flatulent dyspepsia or of attacks suggesting cholecystitis, and there is often a tenderness over the gall-bladder. If the differential diagnosis cannot be made, an operation should be undertaken if the jaundice has not abated in six weeks. So long a wait may risk damage to the liver, but this risk may be less than that of performing a useless operation on a patient dangerously ill with hepatitis. With such a wait an organic obstruction is usually found at operation.

A stone may be impacted in the common duct without causing jaundice; therefore absence of jaundice must never be regarded as evidence that the duct is clear. If a stone is impacted, the duct above usually shows some dilatation and the cystic duct a relatively large lumen owing to the passage of a stone down it; but these changes may be relatively so slight that they are often overlooked. If there is any doubt, the duct should always be palpated from without. It has been said that even very small stones can be felt in this way by the trained finger; but often I have removed from the common duct stones which I had failed to palpate from without. Therefore no operation on the gall-bladder can be considered complete unless the common duct has been explored and the patency of its lumen made evident. Such an exploration, however, may increase the danger of the operation. If in such a case there has never been any jaundice, the cystic duct is small, the common duct is not dilated, and nothing can be felt from without, it may be considered that the risk of overlooking a stone in the duct is less than the risk to the patient of exploring it; and a simple cholecystectomy may be performed, but a note should then always be made that the duct was not explored, and the patient should be carefully watched after the operation.

*Recurrent stones.*—Some of the recurrent stones found in the common duct may have been formed therein after the first operation. This possibility considerably affects the prognosis. If there is a cholangitis and a stone is removed, another may form later, but if it is an overlooked stone, it is improbable that a second will escape notice. A stone formed in the common duct in cholangitis consists of relatively soft pigment calcium and contains no cholesterol, whereas a stone formed in the gall-bladder is laminated. Of the 65 cases of recurrent calculi in my series only nine of those in the common duct were pure pigment, the remainder being laminated stones. Hence I believe that most of the recurrent stones in the common duct have been overlooked at the first operation, and that true recurrences are rare. For this reason I have very little faith in the suggestion that the common duct should be washed out with ether. Ether dissolves pure pigment calculi but has no effect on laminated calculi. It is therefore better always to explore the duct and to dilate the ampulla to allow small fragments to pass.

*Operation.*—A free exposure must always be made. I prefer the right paramedian incision. If the back is slightly arched on the gall-bladder rest, and the foot of the table slightly tilted downwards, good access, especially to the ducts, can always be obtained. Occasionally a transverse incision of the whole thickness of the abdominal wall or of the posterior sheath only may be useful. The Kocher incision I never employ. I am aware that several very experienced and skilled surgeons advocate its use, but I have seen



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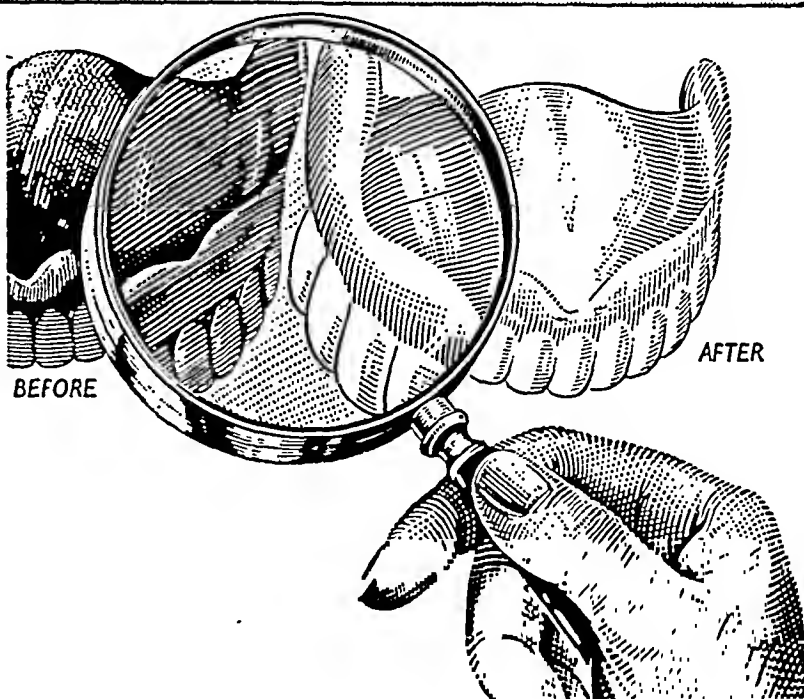
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several large ventral herniæ after its use by other surgeons, and in other cases of recurrent calculi where this incision had been previously employed I have found the upper segment of the rectus atrophic, owing to division of its nerve supply.

The intestines below having been packed off and the gall-bladder drawn upwards and outwards, the peritoneum of the edge of the gastrohepatic omentum is divided, and the ducts are carefully dissected. Usually the three ducts—cystic, common hepatic and common bile—are easily identified; no structure whatever must be divided until all three have been identified. The cystic duct is now divided and clamped; the cystic artery, identified and distinguished from a loop of the right hepatic artery, ligatured and divided. The clamp is slipped from the lower end of the cystic duct, a dissector inserted down it and the duct slit up. It is the usual custom to close the cystic duct and to explore the common duct through a separate incision. As a rule the slitting up of the cystic duct is preferable. Only one opening is made in the duct, and, when it is sutured, no stump can be left to form a new pouch like a gall-bladder—a complication which I have seen in three cases. The only condition in which a separate opening is necessary in the common duct is when the cystic duct is very long and opens into the ampulla. When the cystic duct has been slit up, a pair of very fine forceps is passed downwards, any stone removed (figure 3c), and the forceps then passed through the papilla and opened as widely as possible, so as to dilate fully the opening of the duct. This I regard as the complete operation which is desirable in every case and only to be shortened in those patients who are bad operative risks. Since the routine use of this procedure I have not met with any symptoms due to spasm of the sphincter of Oddi. In a few cases a stone may be so firmly impacted in the ampulla that it cannot be displaced upwards and withdrawn by forceps. A

transduodenal approach with incision of the papilla may then be necessary.

The next question is that of drainage of the common duct. The usual indications for this procedure are: (1) great dilatation of the common duct; (2) recurrent calculi; (3) soft pigment calculi; and (4) pus in the ducts. If the forceps can be passed freely into the duodenum and dilated, many of these cases may be left without drainage. In other words, internal is substituted for external drainage, and I generally only drain externally a duct which contains purulent bile. For drainage I never use a T-tube; its withdrawal is likely to injure the duct, and its use is never necessary. If the bile is very infected, a smooth rubber tube should be inserted up towards the hilum of the liver. If the infection is less, the tube may be passed downwards towards the duodenum, in which case some bile may pass downwards alongside it. The tube should always be fixed in position with a fine intestinal catgut suture and the duct closed round it. It should not be withdrawn until the tenth day. The gall-bladder is now removed, the cut edges of the peritoneum of the gastrohepatic omentum sutured over the stump of the sutured cystic duct or round the tube, and the suturing continued upwards to unite the edges of the gall-bladder bed. Whether the common duct is drained or not, a tube should always be inserted down to Morison's pouch, for in some cases small accessory ducts open directly into the gall-bladder and may discharge a small quantity of bile. This tube can usually be removed in twenty-four to forty-eight hours.

The results of operation show that the impaction of a stone within the common duct must always be regarded as a serious complication. Most of my fatal cases have had symptoms suggestive of liver failure, and it is for this reason that I advocate early operation before the hepatic damage has advanced to a severe degree.

## Reviews

**MINOR SURGERY AND THE TREATMENT OF FRACTURES (HEATH, POLLARD, DAVIES): FOR THE USE OF HOUSE SURGEONS, DRESSERS, AND JUNIOR PRACTITIONERS.** Twenty-second Edition.—By G. Williams, M.S., F.R.C.S. With a Chapter on 'The Administration of Anæsthetics' by H. N. Webber, B.Chir., D.A. 1940. J. and A. Churchill, Limited, London. Pp. viii plus 472, with 283 illustrations. Price, 12s. 6d.

DR. CHRISTOPHER HEATH was born two years before Queen Victoria came to the throne, and at the age of twenty-six he wrote the first edition of this book, which has been the bible of three generations of house surgeons and dressers and is now brought up to date ready to serve a fourth. The book was known as Heath and Pollard in the reviewer's student days, for Bilton Pollard took over the editorship when Dr. Heath died in 1905, and since then the book has passed through ten more editions under the editorships of Mr. Morrison Davies and the present editor. It has also been translated into Chinese.

The book has had many imitators, some more pretentious and many remarkably good, but none have replaced this book in the reviewer's esteem and the reason is not by any means a sentimental one.

The big event since the last edition has been the introduction of sulphanilamides, but, as the editor points out, it is too soon to be sure how far their introduction has modified the procedure for the treatment of septic wounds; so he decided not to make any radical changes on this account, as it is too early to be dogmatic.

Another section where advances have necessitated revision is in the subject of anæsthesia.

The book is still one of the best twelve-and-six-pence worth that the student entering on his term in the out-patient departments and surgical wards can purchase.

**A SHORT TEXTBOOK OF SURGERY.**—By C. F. W. Illingworth, M.D., F.R.C.S. Ed. Second Edition. 1939. J. and A. Churchill, Limited, London. Pp. x plus 707, with 12 plates and 189 text-figures. Price, 21s.

In these days of specialization it takes a great deal of courage to write a textbook on general surgery. Yet the student must have his textbooks, and, to look at it from his point of view, if he is expected to acquire a certain degree of general knowledge on surgery, which is only one of many subjects in his curriculum, surely he can expect an experienced surgeon to be able to broaden his own knowledge sufficiently to write a textbook that will cover the student's requirements.

The author of this textbook is fully conscious of the difficulties of his task; he modestly and very neatly defines the limits of his ambition when he says, 'the most I can hope is that my neurology will satisfy the urologists, my gynaecology the orthopædists'.

The author's courage and industry have been rewarded for he has produced a book that will have an immediate appeal to the student and if he assimilates the contents intelligently he will not only satisfy his examiners, but will have acquired a very sound grounding in surgery that will stand him in good stead when he goes into general practice, or form a firm foundation on which to build special surgical knowledge, should he wish to take higher examinations in surgery.

As this is a second edition, no special criticism of the contents is necessary. No material changes have been made, for the first edition only appeared a year ago.

It is a book very well suited to the requirements of the student in this country and practitioners will find it a useful book of reference.

**MINOR SURGERY.**—By R. J. McNeill Lovo, M.S. (Lond.), F.R.C.S. (Eng.). 1940. H. K. Lewis and Company, Limited, London. Pp. vii plus 369, with 155 illustrations. Price, 12s. 6d.

THIS is a new 'minor surgery'. The author has followed very much the orthodox lines, except that he has pressed into his service a number of collaborators, about which he has given the reader very little information, beyond their names at the beginnings of the chapters they have contributed. In these days of specialization, it is perhaps as well to have the teachings of a number of experts, even on a limited subject like this; skilful editing has ironed out any unevenness in the various contributions.

There are other books which cover the same range of subjects and it is difficult to judge between them. This book, however, is a very satisfactory one. It is easy to handle and slips into the pocket, it provides as complete a guide to practice in the casualty and surgical out-patients as a dresser or house surgeon could wish for, and the price is very reasonable.

The illustrations are numerous and where necessary they are in colour, the binding is strong and is innocent of the varnish which is such a joy to the tropical cockroach, the methods described are practical, and the teaching sound.

**RECTAL SURGERY: A PRACTICAL GUIDE TO THE MODERN SURGICAL TREATMENT OF RECTAL DISEASES.**—By W. Ernest Miles, T.D., F.R.C.S. (Eng.), F.R.C.S.I. (Hon.), F.A.C.S. (Hon.). 1939. Cassell and Company, Limited, London. Pp. xi plus 359 with 105 illustrations. Price, 17s. 6d.

IN his preface the author has stated with modesty that this book 'is nothing more than a record of my personal interpretation of the various problems presented to me by rectal disease and of the methods of treatment which experience has proved to be most efficacious'. It is precisely for these reasons that this little handbook will be readily welcomed by the practising surgeon and the senior student, for the name of Mr. Ernest Miles is linked with notable contributions in this branch of surgery.

It is of no little credit to the author that in a volume of this size, consisting of fifteen chapters, hardly anything of importance has been omitted. It is true that this monograph should not be regarded as a textbook, but as a practical guide and *vade mecum* it has no equal. Desperate diseases may require heroic measures and the greatest surgical skill and courage are called for in the treatment of carcinoma of the rectum. The evolution of the radical abdomino-perineal operation is a case in point. Unfortunately there is a tendency to-day to revert to less radical measures, chiefly with a view to minimizing the rate of mortality. In the hands of Mr. Ernest Miles it has been brought down to the neighbourhood of ten per cent, a great achievement. Anorectal fistulæ comprise a subject beset with many difficulties well known to the practising surgeon, owing to the disastrous consequences of some operative methods. These will be remedied, in a great measure, by the anatomical classification and the rational operative measures advocated by the author. Another noteworthy feature of this book is the clear exposition of differential diagnosis.

The printing, get-up and illustrations are all excellent. An adequate index is appended. We strongly commend this book to the notice of the general practitioner for he cannot afford to be without it.

P. N. R.

**THE STUDY OF ANATOMY.**—By S. E. Whitnall, M.A., M.D., B.Ch. (Oxon.), M.R.C.S., L.R.C.P., F.R.S. (Canada). Fourth Edition. 1939. Edward Arnold and Company, London. Pp. 124

THERE is little doubt that this revised and enlarged edition will be welcomed by all concerned with the study of human anatomy, i.e., both students and teachers.

The book consists of seven chapters of which the first two are mainly devoted to outlining 'the principles' of the subject and 'the practical methods' of study. These two chapters should be read and re-read by every medical student before beginning his own studies of the human body by dissection, if he is to avoid unnecessary memorization of the details. The third and fourth chapters are intended chiefly for teachers on whom lies the most onerous task of directing the student along the proper lines of study most conducive to the realization of essentials of anatomy and of infusing life into the study of the dead.

The fifth and sixth chapters are concerned with directions on 'general reading' and a very useful hint to the younger students in the matter of selecting good 'books' for their studies of human anatomy, as well as such other general books as have stood the test of time for widening their outlook and imagination. In the last chapter will be found not only a very selective list for reference but also a very wholesome suggestion of subjects for collateral reading by students and special studies by more senior students and teachers.

In these days of the crowded medical curriculum, it is difficult to give more than a limited time to any subject. To derive, therefore, the maximum benefit from limited studies of such a fundamental, yet essentially such a vast, subject as anatomy, it should of necessity be a well-designed and methodical procedure from the very beginning, so that the work may be arranged to enable one to obtain a thorough grasp of main facts, and carry the essential knowledge thus gained throughout the course of one's professional studies.

We most strongly commend this book to all medical students and teachers, and, we are confident that a perusal of this book will widen the outlook of the reader, who will have reason at the end of his studies to be grateful to the learned author for such an excellent production.

The publishers' task in the matter of the format, printing and paper has been uniformly satisfactory.

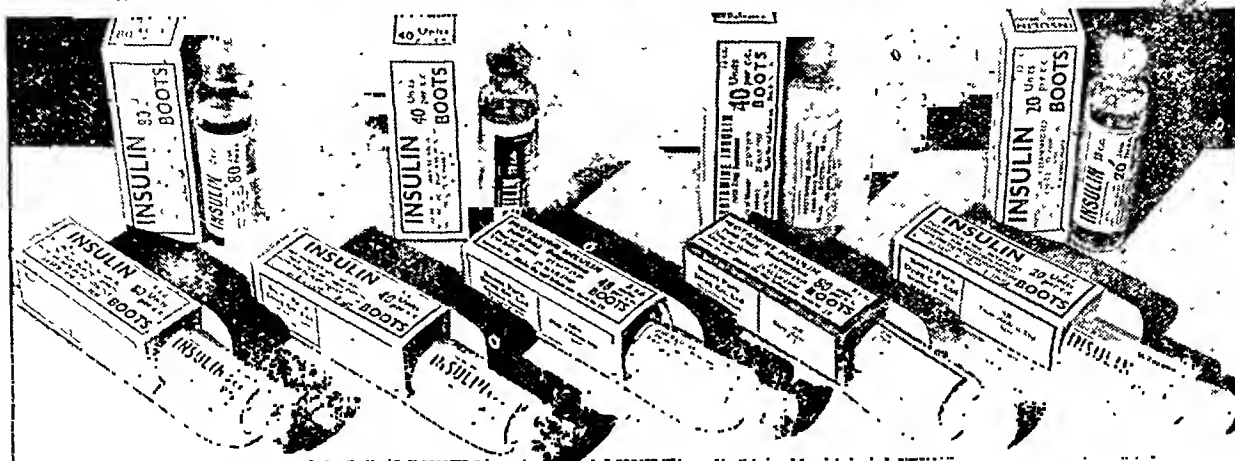
S. C. S.

**PATHOLOGY: AN INTRODUCTION TO MEDICINE AND SURGERY.**—By J. Henry Dible, M.B. (Glas.), F.R.C.P. (Lond.), and Thomas B. Davie, B.A. (Cape.), M.D. (L'pool.), M.R.C.P. (Lond.). 1939. J. and A. Churchill Limited, London. Pp. x plus 931, with 374 illustrations including 8 plates in colour. Price, 36s.

THE publication of an entirely new book on pathology is an important event and teachers in all medical schools where the English language is used will be, or should be, very interested; by this we do not mean only teachers of pathology but of medicine and surgery, for, as the authors of this book emphasize, pathology should be taught as an introduction to medicine and surgery.

The highest aim of medical science should be kept always before the student, and he should be taught to think in both directions; not only must he look forwards from the pathological processes of the active stages of the disease, which he can visualize, either to the stage of repair of the organ or limb, which he still has to visualize, or to the final stage of disease which he can see in the post-mortem room or operating theatre, but also backwards to the process of invasion by the pathological agent, and still further back to the epidemiology of the disease, to the conditions which effect the contact of the human organism with the causal agent or which make the former susceptible to

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the malign designs of the latter, so that he, the student, will always think in terms of prevention as well as of cure.

The authors have kept this ideal well to the fore in their presentation of the subject. They have aimed at presenting a living and progressive picture of the disease processes; they have laid great emphasis on the genesis of disease, so that the physician or surgeon can visualize what is happening inside a patient when he looks at him and makes his physical examination, and the limited pathological examinations that can be carried out during life; and they have for the most part avoided descriptions and illustrations of post-mortem tissues and museum specimens. Finally, they have striven throughout the book not to divorce pathology from clinical medicine and surgery, and in order to keep the student in close touch they have often included short clinical descriptions of the diseases whose pathology they are teaching.

The standard practice of dividing the subject into general pathology and regional pathology has been followed, but between these two sections a section on special infections has been interposed. This section is not just a treatise on bacteriology or parasitology, for it deals with the reactions of the body to the infections rather than with the organisms themselves, and further it is not comprehensive but aims at giving type infections. No descriptions of animal parasites have been included, and the reasons the authors give for this are rather poor, namely, that they illustrate no special principles in pathology, and that they are so well described in books of parasitology. The first, if our interpretation of the meaning of the sentence is correct, is not true, and the second could be applied to many subjects dealt with in the book.

There are two excellent chapters on diseases of the blood. The story of the evolution of our present knowledge on pernicious anæmia is particularly good; the recent work on the pathology of the stomach in this disease is included; in fact more than this, it is repeated, for figures 193 and 282 are identical. More recent observations regarding the pernicious anæmia of infection with *Diphyllobothrium latum*, or *dibothriocephalus latus* as the authors write it, question the causative connection between the anæmia and the helminthic infection: both pernicious anæmia and this particular helminth are common amongst Finns, and the association may be accidental.

The authors have taken many of the illustrations of blood cells from Whitby and Britton's book and it is a pity they did not also take more of their principles of hæmatology. They give the hæmoglobin in a typical normal blood count of a man of 45 as 95 per cent—Haldane (which in terms of grammes of hæmoglobin per 100 c.cm. of blood is 13.1) and we know of no country where this can be considered the average amount; in most countries it is at least 2 grammes higher than this. Nor do we consider that 2.0 mgm. (4 units) of bilirubin in the blood could be considered anything but pathological.

The authors are professors of pathology at the universities of London and Liverpool, respectively, and are therefore both experienced teachers, and they have presented the subject in a rational, clear, and interesting manner. Their book should make a very useful textbook for the student and we strongly recommend it to the teacher in this country. There are a few mistakes, in facts as well as in figures, but these will undoubtedly be corrected in subsequent editions, and even as it stands the book is a very important contribution to the teaching of medicine, in its widest sense, and we foretell a bright future for this new venture.

**VADE MECUM OF MEDICAL TREATMENT.**—By W. Gordon Sears, M.D. (Lond.), M.R.C.P. (Lond.). Second Edition. 1939. Edward Arnold and Company, London. Pp. vii plus 376. Price, 10s. 6d.

The fact that the author has found it necessary to produce a second edition of this book in just over two years bears testimony as to its growing popularity and usefulness.

The book provides in a convenient form and handy size an excellent synopsis of medical treatment of all diseases commonly met in general practice. The contents are generally arranged in alphabetical order to facilitate ready reference. The appropriate lines of treatment for a particular case should be selected by the practitioner from the different therapeutic procedures given in this book, which are based on the author's personal experience and information taken from recent literature and standard books. Occasional reference has been made to methods and points of diagnostic importance.

In addition to the various modern lines of treatment already referred to in the previous edition, the present volume includes the main advances in therapeutics, e.g., chemotherapy, in the form of the sulphanilamides and allied drugs and zinc protamine insulin. A few useful tables have been added in the appendix.

The book will continue to be a valuable guide to treatment in general medical practice.

M. N. R. C.

**INDIGENOUS DRUGS OF INDIA: THEIR SCIENTIFIC CULTIVATION AND MANUFACTURE WITH NUMEROUS SUGGESTIONS INTENDED FOR EDUCATIONISTS AND CAPITALISTS.**—By J. C. Ghosh, B.Sc. (Manchester). Second Edition. 1940. Published by P. K. Ghosh, School of Chemical Technology, Calcutta. Pp. xvi plus 243. Price, Rs. 3 (postage extra). 5s. 6d. (postage free).

THE first edition of this handbook was published in 1919 and consisted of a series of independent pamphlets on the subject of pharmaceutical industries in India. While this edition has been thoroughly revised and considerably enlarged, the original plan has been generally retained and an attempt has been made to stimulate the interest of the reader in the scientific cultivation, manufacture and use of the Indian indigenous drugs.

Having had the advantage of being associated with a large manufacturing establishment in India, Mr. Ghosh is fully aware of the needs and also the latent possibilities that exist for the development of new pharmaceutical industries in this country and has presented all these technical facts together with his personal experiences in a readable and interesting manner which should provide food for thought to all those who are keen to see India become independent in the matter of her drug supplies from foreign countries.

The book is divided into three main chapters and three appendices. In chapter I, the scientific and commercial aspects of drug cultivation and the problem of drug adulteration and spurious drug trade in India are described. The author has maintained that India with her vast resources of vegetable materia medica should be in a position not only to supply her own needs but should be able to export substantial supplies to foreign countries. The reason why India is still largely dependent on imports is, according to the author, the fact that adulteration and tampering with the quality of crude drugs has been the rule rather than the exception in the Indian drug market—a view with which the reviewer finds himself in general agreement. To remedy this situation, Mr. Ghosh has strongly advocated the enactment of an all-India Drugs and Pharmacy legislation. Here again, the author will find many in India to fall in line with his view-points. In chapter II, the author has given brief notes on the pharmaceutical and therapeutic aspects of a few Indian indigenous drugs such as aconitum, ajowan, *Allium sativum*, aloes, *Atropa belladonna*, *Hydnocarpus wightiana*, etc., which he himself studied. The information contained herein is however of a very preliminary nature. Chapter III deals with the market facilities for crude drugs in London and elsewhere. The data given are interesting but do not appear to be of much technical value from the point of view of drug dealers.

Of the appendices, appendix I, containing a list of vegetable drugs with their natural orders, habitat, and therapeutic uses, and their vernacular equivalents in

nine languages, should be of particular value for reference purposes. In appendix II, a set of useful prescriptions is given with the idea that these will be 'particularly useful to mofussil and other people wanting cheap and easily available medical aid'. The information given here is certainly not enough to guide laymen and the reviewer feels that this sort of meagre treatment of a subject may do more harm than good by encouraging self-medication. This appendix again is not quite relevant to the theme which the author has in mind and could easily have been omitted.

The author deserves congratulation for bringing to the forefront, in a low-priced easily-readable handbook, a subject which is of paramount importance to a poor country like India, particularly at this time when an acute shortage of drugs due to supplies being cut off on account of the war is already evident. The problem of supplying India's 400 million people with drugs and medicinal chemicals can only be solved by utilizing India's indigenous drug resources and developing indigenous drug industries, as Mr. Ghosh has advocated. Industrialists may find a lot of useful hints from a perusal of this book.

B. M.

**DIAGNOSIS AND MANAGEMENT OF DISEASES OF THE BILIARY TRACT.**—By R. Franklin Carter, B.S., M.D., F.A.C.S., C. H. Greene, A.B., Ph.D., M.D., F.A.C.P., and John Russell Twiss, A.B., M.D., F.A.C.P. 1939. Baillière, Tindall and Cox, London. Pp. 432. Illustrated with 84 engravings with 6 plates. Price, 32s. 6d.

THE authors are members of the professorial staff of the New York Post-graduate medical school, and their book is based on their experience with diseases of the biliary tract over a considerable period of time, especially at their hospital's clinic for the study of diseases of the liver and biliary tract.

The preface promises a concise description of the latest concepts of the ætiology of diseases of the gall bladder and the routine of investigation and management as practised at this clinic. This is accomplished in the short space of four hundred pages with great success.

The opening chapters discuss the current opinion on various ætiological factors, and they serve to show how much has yet to be clarified despite the constant interest that is being taken in these problems throughout the world.

For example, a review of the theories regarding gall stone formation shows that no single factor can be responsible for their causation, but that biliary stasis is probably of most importance. The difficulty lies in the probability that, by the time a gall stone has appeared, the conditions determining its deposition have altered.

The second part is concerned with the investigation of patients. The technique of duodenal drainage is described in detail, and the significance of the findings explained.

The Twiss tube, as used at this clinic, is at present the most reliable method of obtaining bacteriologically uncontaminated specimens of bile from the duodenum, and the results that are being obtained deserve attention. Other methods of investigation are described, and mention must be made of intravenous cholecystography, described by Dr. Hubbard Lynch.

Two admirable sections follow, describing respectively medical and surgical treatment, and it is not easy to single out passages for special comment. In the medical section the diet sheets are adaptable to the needs of patients in this country, and in the surgical section we all have something to learn from the articles on the selection of patients for operation.

Wider aspects of surgery in relation to biliary tract disease occupy part V, and finally space has been found for an appendix containing various useful tables.

A carefully written and authoritative work, this book should be in the hands of everyone interested in the subject.

W. McN. N.

**ASTHMA.**—By Frank Coke, F.R.C.S. With the collaboration of Harry Coke, M.R.C.S., L.R.C.P. Second Edition. 1939. John Wright and Sons Limited, Bristol. Pp. xii plus 266. Illustrated. Price, 15s.

THE authors have tried to face squarely all the factors involved in the production of the clinical syndrome—asthma. They have strongly advocated the use of the differential sedimentation test in classifying the factors into three main groups and throughout this book these three types have been referred to, emphasized, and reiterated. The book contains abundant interpretative material and expressions of personal observation and experience. The chapter on allergy is exhaustive; the value of treatment on bacteriological lines has been fully emphasized. The book contains extensive discussions on the intractable forms of asthma and records of gratifying success after treatment.

The chapters on other complaints allied to asthma, such as hay fever, urticaria, migraine, rhinitis, angioneuratic oedema, eczema, cyclical vomiting, epilepsy, and angina pectoris, have been dealt with shortly. The authors have, however, effectively revealed the urgency of losing no hope in dealing with asthmatics.

G. N. S.

**FUNCTIONAL DISORDERS OF THE FOOT: THEIR DIAGNOSIS AND TREATMENT.**—By Frank D. Dickson, M.D., F.A.C.S., and Rex L. Diveley, A.B., M.D., F.A.C.S. 1939. J. B. Lippincott Company, Philadelphia and London. Pp. x plus 305, with 202 illustrations. Price, 21s.

THE title of this book is apt to be misleading, because all the disorders of the foot which it describes have an essentially organic basis.

The preliminary section on morphology and anatomy is largely taken from the work of D. J. Morton, whose opinions diverge in some respects from those of English writers, such as Keith and Lake. Although Morton argues against the existence of an anterior transverse metatarsal arch, the authors of this book take sides with the majority in assuming that this arch does in fact exist.

Foot imbalance in childhood, adolescence, and adult life is then discussed. Stress is laid on the occurrence of foot imbalance in childhood as a factor in producing the structural defects that underlie most of the foot troubles of adult life.

Treatment is described in the appropriate chapters, with modifications according to the age of the patient. It is directed towards the increase of tone, correction of short tendo achillis, the modification of footwear, the use of arch supports, and, lastly, operation. A type of non-rigid support designed by the authors is described.

It has the great advantage that the surgeon himself can fit the support to the patient's foot in the space of a few minutes.

The last part of the book describes diseases of the integument and small bones that cause painful feet; the list of omissions from this section is long. Finally comes a useful section containing illustrated notes on strapping and foot exercises.

The book has been well published, with clear illustrations and in an exceptionally readable form.

W. McN. N.

**THE MECHANISM OF THE HUMAN VOICE.**—By Robert Curry, M.A., Ph.D. 1940. J. and A. Churchill, Limited, London. Pp. ix plus 205, with 20 illustrations. Price, 10s. 6d.

THE author covers a very large field, commencing as he does with the nature and development of voice, as illustrated in the lower animals, and finally he traces it up to the complex human voice. The development is clearly and methodically worked out. Following the chapters on development, the details of anatomy of the vocal organs are dealt with, including all the recent work in this line. Dealing with the motor organs chiefly



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concerned, the author describes the larynx and its adjuncts and describes in detail the anatomy and physiology of these parts and the possible action or actions of the larynx as a vibrating system in the production of voice. The function of the psychic centre for speech, the manner in which afferent impulses are enabled to influence its action are briefly discussed in connection with the function of cerebrum and cerebellum. The cortical control of the voice has been the subject of dispute among many authorities; the author has discussed the points and is of opinion that the paracentral gyrus, the posterior, triangular or orbital parts of the inferior, frontal gyrus and the superior, middle and inferior temporal gyri are the controlling centres for speech.

The allied function of hearing too is not neglected and brief outlines of the anatomy and physiology of hearing and its important relationship to voice is discussed. Although the technique of analysing sound has not reached a stage of perfection, the author has given an interesting account of the more important experimental methods. Lastly, the disorders of voice and speech have been studied from different view-points and the author has based the abnormal state upon anatomical, physiological, and psychological and linguistic defects.

The author brings to his task experience of many years as a student of physics, phonetics, psychology, anatomy, physiology, and laryngology. He has ably marshalled the facts and has presented both sides of arguments in controversial matters and has drawn his conclusion in a logical manner. The result is a book of first importance that fills a real need in medical literature and will be recognized as an authoritative work of reference to physicians, scientists, and teachers of elocution. It contains an extensive bibliography. The book is profusely illustrated. Though small in size, it is worth its price for the vast amount of information concentrated in such a small volume.

M. N. D.

**A TEXTBOOK OF BACTERIOLOGY: THE APPLICATION OF BACTERIOLOGY AND IMMUNOLOGY TO THE AETIOLOGY, DIAGNOSIS, SPECIFIC THERAPY AND PREVENTION OF INFECTIOUS DISEASES FOR STUDENTS AND PRACTITIONERS OF MEDICINE AND PUBLIC HEALTH.**—By H. Zinsser, M.D., and S. Bayne-Jones, M.D. Eighth Edition, 1939. D. Appleton-Century Company, Incorporated, London. Pp. xxviii plus 990. Illustrated. Price, 30s.

This book has a thirty-year reputation as a sound book on bacteriology, falling somewhere between the students' handbook and the complete encyclopædia on the subject. Hiss and Zinsser was a reference book that was frequently found in the army bacteriological laboratories during the last war; these books were probably the second and third editions, and we have no doubt that the eighth edition will be found just as frequently in the corresponding laboratories in this war.

By this we do not mean to suggest that it particularly deals with war conditions, but that under service conditions libraries had to consist of only one or two books, and one could nearly always find anything on the theory or practice of laboratory work associated with the micro-organismal agents of human disease in this book. For this reason, but for this reason only, it is perhaps a pity that the section on protozoa is omitted. The reasons given for this omission include the very obvious one that protozoa are not bacteria and that they have their own literature, and, secondly, the very honest reason that the authors don't know enough about the subject; a fact that so seldom deters writers of this type of book.

If protozoa have been left out, organisms on the smaller side of the scale, rickettsiæ and viruses, have received their fair share of attention; in fact, the section on rickettsia is one of the best in the book.

Recent work on virus diseases has necessitated considerable additions to this section; our knowledge has both extended, that is to say more diseases are now recognized as ultra-microscopic virus diseases, e.g., influenza, and becomes more precise, for we now know many facts about viruses which distinguish them one from another. All the recent work on yellow fever has been added in this edition, including reference to protective vaccine now made by growth on chick embryo.

This is perhaps the most *readable* of all books on bacteriology. Professor Zinsser has a delightful literary style which continually peeps through the sober presentation of facts which naturally forms the substance of a scientific work. His admirers will welcome this new edition and those who were previously unfamiliar with it will be delighted with their new experience. It is a book to be recommended, unconditionally.

**A NEW DICTIONARY FOR NURSES.**—Compiled by Lois Oakes, S.R.N., D.N. (Lond. and Leeds). Assisted by Thos. B. Davie, B.A., M.D. (Liverpool), M.R.C.P. (Lond.). Sixth Edition, 1940. E. and S. Livingstone, Edinburgh. Pp. xx plus 410. Illustrated. Price, 3s. Postage 2d.

This is a very complete vocabulary of medical terms as required by nurses; it also contains a useful summary of diets and nursing technique, and is strongly to be recommended for both student and qualified nurses.

C. F.

**AIDS TO ANATOMY AND PHYSIOLOGY FOR NURSES.**—By Katharine F. Armstrong, S.R.N., S.C.M., D.N. (Lond.). 1939. Baillière, Tindall and Cox, London. Pp. xii plus 384, with 163 figures. Price, 3s. 6d.

This is a valuable summary of the subject, and should prove very useful to nurses revising their knowledge and as a sound basis for their medical and surgical lectures.

C. F.

## Abstracts from Reports

### REPORT ON THE STATE OF PUBLIC HEALTH IN BURMA DURING 1938

#### VOLUME I

##### *Principal diseases*

In Burma the major epidemic diseases are cholera, plague and smallpox. These diseases are so well known that villagers are able to distinguish them easily and report their incidence to headmen. The improvement of sanitation and the protection of public health including the prevention of the spread of contagious and infectious diseases among human beings are the responsibilities of the local bodies both in rural and

urban areas. While a few of the municipalities have a staff sufficient to deal with an outbreak of epidemic disease, the district councils have to depend upon this department for the provision of qualified medical personnel for taking the necessary preventive measures.

**Cholera.**—This disease was not prevalent during the year. The provincial death rate was 0.05, which is below the previous year by 0.24 and the five-year mean by 0.15. Seventy out of the 106 deaths from cholera recorded in the urban areas were in Toungoo where the disease appeared in epidemic form, the cases in the other 11 towns being of a sporadic nature.

**Plague.**—The number of deaths due to plague is the highest since 1929 and the death rate 0.38 shows an



increase of 0.25 compared with the previous year and 0.24 over the five-year mean.

**Smallpox.**—The death rate from smallpox, 0.02, is the lowest for the past 22 years. It is below the previous year's figure by 0.09 and the five-year mean by 0.10. Mortality was reported from 19 out of 31 districts. The largest number of deaths took place in April and the least in October.

**Enteric fever.**—This is a notifiable disease in all towns in Burma. The health officer has to depend mainly on private practitioners and doctors in charge of hospitals to furnish him with information regarding morbidity. Apart from admissions into hospitals, the number of cases reported by medical practitioners are few. It is not therefore possible to furnish the number of persons down with this disease. With regard to deaths, the health officer or medical registrar has in most cases to rely on the history given by the relatives of dead persons and on the examination of dead bodies. Under the circumstances the mortality figures can at best be taken to indicate only the relative prevalence of the disease.

During 1938, 451 deaths were recorded and the death rate of 0.32 is less than the previous year by 0.01.

**Dysentery and diarrhoea.**—These accounted for 6,400 deaths during the year. The death rate is 0.53, which represents a decrease of 0.05 below the previous year but an excess of 0.05 compared with the five-year mean. The largest number of deaths took place in the month of July and the least in March.

**Respiratory diseases.**—The number of deaths ascribed to this group of diseases is 14,297 and the death rate of 1.8 shows a rise of 0.03 compared with the previous year and 0.11 compared with the five-year mean. The rate for rural areas is 0.32 and that for towns is 7.70. Of the 10,871 deaths recorded in towns under this head, 4,685 were ascribed to pneumonia, 2,757 to pulmonary tuberculosis, 15 to whooping cough and the balance to other respiratory diseases. These figures indicate that pneumonia and pulmonary tuberculosis were responsible for the major portion of the deaths.

**Beri-beri.**—There has been a marked rise in the incidence of this disease during the year.

The total number of deaths recorded from this cause in towns was 460 and the rate 0.33 is the highest for the past nine years. The Health Officer, Rangoon Corporation, reported 534 attacks and 265 deaths. The disease was mostly confined to the Indian community, the Telegus from South India being more prone to beri-beri and the Mohammedans from Bengal and Chittagong to epidemic dropsy. Other towns recording a large number of deaths were Moulmein 34, Nyaunglebin 32 and Mergui 26.

**Cerebro-spinal meningitis.**—Reports were received about the continued prevalence of this disease in the early part of the year in the Haka subdivision in the Chin Hills district. Cases occurred in three villages. In the Upper Chindwin district six cases with six deaths were reported from Layshi village in Somra tract. The situation needs watching. In the towns of Burma 51 deaths were recorded, of which 39 were in Rangoon.

**Malaria.**—Burma like other tropical countries has its problem of malaria to contend with. The disease is extensively prevalent and causes much sickness and mortality especially in the rural areas. Unfortunately we have no reliable data to gauge its prevalence in villages, where the headmen who act as registrars cannot differentiate the various kinds of fever. From blood counts and spleen censuses taken in various places in Burma, the Malaria Bureau, at the Harcourt Butler Institute of Public Health has been able to distinguish regions where malaria is endemic from regions where it is only slightly prevalent. In the year under report fevers accounted for 38.39 per cent of the total mortality. In the opinion of public health and medical officers who have opportunities to observe the mortality caused by malaria, half the deaths ascribed to fevers in rural areas may be taken to be due to malaria. On this basis, approximately 57,000 deaths in villages this year were due to malaria.

**Leprosy.**—The number of deaths due to leprosy in towns during 1938 was 353, the rate being 0.25. By far the largest number was recorded in Rangoon 136, Mandalay 59 and Moulmein 20. The existence of leper asylums in these places has been mainly responsible for the large number recorded. The disease is made notifiable only in Maymyo and Mōnywa Municipalities; hence there are no reliable statistics to judge its incidence in urban areas; and in respect of rural areas even mortality figures are not available.

As a result of the appeal issued by His Excellency the Governor of Burma in December 1937, a central association with a strong and influential executive committee was formed with the object of controlling tuberculosis and leprosy. Up till the end of the year a sum of Rs. 4,50,681-7-11 has been collected and vested in a Board of Trustees.

The Director of Public Health, Burma, furnished the association with an outline of work for combating leprosy. The services of an expert in the person of Dr. J. Lowe, M.D., Leprosy Research Worker of the Indian Council of the British Empire Leprosy Relief Association were obtained.

His report has thrown valuable light on the distribution and incidence of leprosy in Burma. From a study of statistics and other records he remarks that there is probably a belt of country showing a high incidence of leprosy extending across the middle of the province starting with the Chin Hills and Hill Tracts of Arakan and Akyab in the west including most of the southern part of Upper Burma and finishing with the Southern Shan States in the east. A second zone showing a moderately high incidence of leprosy is in the Delta, northern part of Burma showing relatively little leprosy, and the coastal areas showing still less. The type distribution of cases in Burmans differs markedly from that of Indians domiciled in Burma or India and that in Burmans cases of infectious or lepromatous type form a much higher proportion of the total. The high percentage of children infected with leprosy points to the fact that the disease is spreading.

**Tuberculosis.**—It is not possible to judge the extent of prevalence of this disease in the rural areas but in towns 3,016 deaths were recorded under this head during the year. Of these, 2,757 were due to pulmonary tuberculosis, 9 to tuberculosis of joints and the rest to other tuberculous diseases.

The death rate from pulmonary tuberculosis has been steadily on the increase since the year 1920, when figures in respect of this disease were available for the first time. In 1920 it was 1.13, in 1927 1.64, in 1937 2.05 and this year 1.95.

**Yaws.**—From time to time evidence has been accumulating as to the areas in which this disease is rampant in Burma but measures for its eradication were not put into operation on an extensive scale on account of the cost involved in the treatment of cases.

#### ANNUAL REPORT OF THE ALL-INDIA INSTITUTE OF HYGIENE AND PUBLIC HEALTH, CALCUTTA, 1938

RESULTS of practical value have been achieved in investigations into the causation of epidemic dropsy—a disease widely prevalent in the eastern provinces of India, where it is popularly, though erroneously, known as *beri-beri*. Simple tests have been evolved with which it is now possible to detect the poisonous oil, which has been found closely associated with the disease. The poisonous substance in the oil, too, has been followed to its source, to a weed called *Argemone mexicana*, but popularly known as *Kata Kar*, *Stal Kanta* and *Odissimari* in different parts of the country.

The seeds of this weed, which resemble the black variety of mustard seeds, somehow find their way into the stocks of the latter and constitute a poisonous element in mustard oil. The weed can easily be recognized even by the villagers because of its peculiar thorny leaves and yellow flowers and should be removed from mustard fields to prevent contamination



# The Value of Dietary Supplements

*A Summary of Investigations\* published in the "Medical Officer," March 30 and April 6, 1935*

A NUMBER of children, all receiving their customary home diet, were given either No Supplement, Cod Liver Oil, Halibut Liver Oil (with milk to provide equal calories) or Virol. The experimental scheme provided that each child should have a period on each treatment in turn, in such a way that every possible sequence was included. Rigid statistical control was thus possible.

Gain or Loss in Weight on Various Supplements :—

Supplement	Total gain in ozs. over all periods	Average gain per child per week in ozs. over all periods	Total loss in ozs. during summer period only	Average loss per child per week in ozs. during summer period only
No Supplement - -	88	0.3	— 103	— 1.4
Cod Liver Oil - -	287	1.0	— 77	— 1.1
Halibut Liver Oil with milk - - - -	333	1.2	— 184	— 2.6
VIROL - - - -	762	2.6	— 7	— 0.1

Whereas earlier investigations had shown that the mere addition of vitamins had no effect on growth, these investigations have conclusively proved that Virol—a balanced food containing all the necessary vitamins—has a definite and remarkable effect in bringing the rate of growth up to the recommended standard. Virol was the only one of the supplements used that promoted this ideal rate of growth.

Virol was the one and only preparation that maintained the children's weight in the hot weather.

\* The full report will be sent on application to Messrs. A. H. Wheeler & Co., Sudama House, Witter Road, Ballard Estate, Bombay.

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of the oil seeds. Regular examination of stocks of mustard seeds in shops and mills should also go a long way in preventing expression of the poisonous oil and frequent examination of mustard oil exposed for sale should check the use of undesirable supplies for cooking purposes.

Investigations at the institute have shown that rats cause epidemics of severe diarrhoea and certain obscure fevers resembling typhoid. A high percentage of rats has been found to carry infection, and the pest must be systematically destroyed even in the absence of plague, and food, through which infection is carried to man, must be carefully protected from it.

Investigations have also shown that a mild form of scurvy is one of the ways in which the body is left damaged by malaria and that lime juice is a good remedy. The principle has been applied in the new treatment, of black-water fever evolved at the institute which has so far proved successful.

It has been observed, that there is, in epidemics, a preponderance of one type of malaria parasite over another. It is now possible on the basis of this finding to forecast the probable incidence of the disease.

A survey has been made in selected localities of the diets taken by different communities and it has been found that though, as a rule, people who can afford to spend reasonable amounts on food and obtain proper nourishment, this may not always be the case and useful indications have been obtained of the directions in which food in certain communities needs correction.

With the help of an apparatus evolved at the institute, with which it is possible to study the effect of light on the deeper membranes of the eye, it has been shown that as many as 17 per cent of men taking what is called an adequate diet and 43 per cent of those taking a poorer diet show signs of deficiency. Only in 16 per cent of the latter group was external evidence of deficiency diseases manifest. Most of them made rapid recovery when the element which was deficient in their diet was supplied.

A simple method has been worked out of studying the structure of the teeth, which gives indications of efficiency in the assimilation of lime by the human being, and the milk-teeth of children when they drop out, can now be utilized for a study of the nutritional history of the child.

Active research is being carried out to discover the causes of high incidence of tuberculosis in the jute industry. The incidence of tuberculosis of the lungs was found to be as high as 2 per cent amongst workers in a jute mill near Calcutta, with an additional 5 per cent or more of probable cases. The seriousness of the problem can be gauged from the fact that industries such as this attract labourers from far and wide and since the labourers return to their villages suffering from tuberculosis, they form a fruitful source of infection for the non-immunized population of the rural areas.

#### ANNUAL REPORT OF THE EXECUTIVE HEALTH OFFICER OF THE CITY OF BOMBAY FOR 1938

THE conditions of public health of the city during the year were not so satisfactory as they should have been. Smallpox which was prevailing at the end of the preceding year assumed an epidemic form at the commencement of the year and the epidemic lasted till the middle of May. This epidemic was soon followed by an epidemic of enteric fever which continued till the end of the year, although the number of cases showed a decline from the month of October.

The number of live births registered was 36,748, being 1,293 more than in 1937 and 6,738 more than the average of the last ten years (1928-37). The birth-rate calculated on the census population of 1931 was 31.6 births per 1,000. The total number of deaths from all causes was 35,999, being 5,231 more than in 1937, 7,092 more than the average for the last five years (1933-37) and 8,608 more than that for the

preceding decennium (1928-37). The death rate per 1,000 of census population of 1931 was 31.0 as against 26.5 in 1937 and 22.8 the rate recorded for the decennium (1928-37). Thus the number of births during the year was more by 749 than the number of deaths. This excess of births over deaths was equivalent to 0.6 per 1,000 population calculated on the census of 1931 and was recorded eight times in succession. Before 1931 there was no such excess since 1866, the year in which birth records were instituted.

There was no death from plague during the year as against 46 the average of the last ten years (1928-37).

Smallpox was in an epidemic form during the first half of the year and caused 1,862 deaths as against 688 in 1937 and 941 the average for the last decennium (1928-37).

Cholera caused one death (the case was imported) against 4 in 1937 and 21 less than the average for ten years (1928-37).

Influenza was prevalent in a mild form in the city during the year and caused 80 deaths as against 68 in the preceding year and 71 the average for the last decennium (1928-37).

The deaths from diseases of the respiratory system numbered 13,584, being 2,343 more than in 1937 and 3,710 more than the average of the last ten years (1928-37).

Tuberculosis accounted for 2,078 deaths as against 2,037 in 1937 and 1,710 the average for the preceding decennium (1928-37).

One hundred and three deaths were due to malaria, being 30 more than in 1937 and 32 less than the average of the last decennium (1928-37). There were 1,065 deaths from ague and remittent fever as against 1,298 in 1937. The average number of deaths for the last ten years (1928-37) from malaria was 135 and from ague and remittent fever 1,373.

The deaths among infants under one year of age numbered 9,801 against 8,688 in 1937 and 7,856 the average for the last ten years (1928-37). The rate of infant deaths per 1,000 births registered was 267.0 as against 245.0 for the preceding year and 261.8 the mean for the preceding decennium (1928-37).

#### THE REPORT OF THE CHIEF ENGINEER, PUBLIC HEALTH DEPARTMENT, BENGAL, FOR THE YEAR 1938

REVIVAL of the policy of making grants-in-aid towards sanitary engineering schemes of local bodies gave a definite impetus to local self-governing institutions to undertake such schemes. Although, owing to the absence of a sufficient number of mature schemes, the total expenditure on such schemes during the year under review was less than during the previous year, there was a distinct rise in the estimated cost of projects taken up during the year.

The total capital expenditure on water-works and sewerage works constructed or under construction during the year under review amounted to Rs. 5,99,816 and Rs. 1,46,097, respectively, as against Rs. 7,50,326 and Rs. 52,027, respectively, during the previous year.

There were 53 water-works in operation in the province under the control of the department during the year under review. The total number of persons served was 1,342,467 and the total quantity of filtered water supplied, 17,748,042 gallons. The quality of water supplied from the various water-works was, on the whole, satisfactory.

Besides the valuable assistance rendered to municipalities and other local bodies in the shape of inspection and advice, new works of sanitary engineering, numbering 20, were executed under the supervision and control of the department during the year. The improvement of rural water-supply was one of the most important activities of the department. A rural water-supply subdivision, consisting of one assistant engineer and three supervisors, was created towards the end of the previous year. The assistant engineer-in-charge of the subdivision inspected several places in the

province in order to make arrangements for water-supply by tube-wells in rural areas. A leaflet on iron eliminators was prepared and circulated. The assistant engineer also made an extensive tour in the district of Bakarganj to investigate the possibilities of water-supply by tube-wells in rural areas. The data elicited during the tour will be of value in the preparation, already undertaken, of a comprehensive water-supply programme for the district.

The schemes of water-supply by means of tube-wells in rural areas formulated by district boards and the prospects of water-supply by tube-wells in such areas out of the grants made by the Government of India as well as the provincial grants and loans were examined by the Public Health Department and necessary reports were sent to district boards and to Government.

The department also rendered valuable assistance to Superintendents of Police on specific problems relating to the improvement of tube-wells in rural thanas.

In several parts of Eastern Bengal the water yielded by village tube-wells is so heavily impregnated with iron salts, and in some cases also with manganese, as to be practically undrinkable. For this reason, ring or masonry wells have proved more popular in these areas than tube-wells, although the water yielded by the former is often of doubtful quality. To remedy this, designs of various economic types of iron eliminators for use with village tube-wells were prepared by the department and experimented upon in several places; and a simple type has been now evolved and placed on the market.

#### THE ANNUAL REPORT OF THE DIRECTOR OF THE PASTEUR INSTITUTE OF SOUTHERN INDIA, COONOR, FOR THE YEAR ENDING 31ST DECEMBER, 1938

RADICAL alterations in the administration and organization of the laboratories were commenced during the year. The course of action was necessitated by a variety of factors among which may be mentioned the continued demands for increased quantities of antirabic vaccine, the ever-increasing volume of specimens sent for laboratory examination, and the fact that the accumulation of reference works and periodicals had outgrown the space available in the original library. Adequate laboratory accommodation had also to be provided for the newly appointed rabies research officer.

During the year under review 406 patients underwent a full course of antirabic treatment at the institute. Of these, 36 were Europeans and 370 Asiatics, figures which showed a decrease of 20 in the total number treated as compared to the previous year.

Incomplete courses of treatment were also given to 82 patients. Of these, 44 were absconded from further treatment as the animals under suspicion remained alive and well for an observation period of 10 days thereby excluding rabies. The remaining 38 absconded. The proportion of absconders to the total treated (complete and incomplete) was 7.8 per cent.

One death from rabies occurred among the Asiatic patients treated at the institute. This patient had received a full course of treatment.

Paris fixed virus was used exclusively in the preparation of the vaccine. It was in its 1011th passage at the close of the year. The vaccine used was a 5 per cent carbolized sheep-brain suspension prepared by Semple's method.

During the year, 16,172 courses of antirabic vaccine were issued to the subsidiary centres, a figure which shows an increase of 801 courses as compared to the previous year.

The number of deaths from rabies among all treated cases (complete and incomplete) was 20, giving a mortality rate of 0.17 per cent. Of the 20 deaths from rabies 8 or 0.07 per cent occurred among the patients who had received a full course of treatment and 12 or 0.49 per cent among those whose courses of treatment were not completed. In the latter group, seven patients developed rabies while receiving treatment and the other five occurred among absconders.

Antirabic vaccine is also available for the prophylactic treatment of animals. While it is advocated that dogs should be protected before they are exposed to infection, it is found in practice that treatment is comparatively seldom given until the animal is at risk. During the year, 40,831 c.c.m. of 5 per cent carbolized sheep brain vaccine were issued for the treatment of animals, chiefly to veterinary officers in the Madras Presidency and neighbouring Indian States.

The number of routine laboratory examinations which the institute performed on behalf of hospitals, dispensaries and medical practitioners continued to show an increase. The total number of such examinations carried out during the year was 4,756. Work of this kind covers a wide field and includes examinations of a hæmatological, serological, pathological, bacteriological and biochemical nature.

The institute also continued to receive, examine and report upon brains from suspectedly rabid animals. During the year, 414 such specimens were received. No charge is made for this service and, where necessary, the results are communicated by telegram free of charge.

Some experiments were carried out on the cultivation of rabies virus in tissue culture. Attempts to cultivate rabies virus on the chorio-allantoic membrane of the developing hen's eggs were unsuccessful.

Towards the close of the year some preliminary experiments were commenced with the object of improving the antirabic vaccine at present in use. The present vaccine while satisfactory from the point of view of a low associated mortality among treated cases is far from satisfactory in respect of the dosage and duration of treatment.

A research unit known as the 'Protozoal Parasites Enquiry' was attached to the institute during the year and is under the control of the director. This unit is entirely financed by the Indian Research Fund Association and is the first of its kind that has come under the direct control of the director of the institute. The work of the enquiry during the short time available before the end of the year was taken up chiefly in establishing colonies of experimental animals, strains of parasites, etc., and no results of importance were obtained. The future programme of study of this enquiry will be devoted mainly to the investigation of immunity to malaria and other protozoal diseases.

#### THE FOURTEENTH ANNUAL REPORT OF THE RANCHI INDIAN MENTAL HOSPITAL, KANKE, IN BIHAR, FOR THE YEAR 1938

THE hospital continues to receive patients from the Provinces of Bengal, Bihar and Orissa.

The sanctioned accommodation of the hospital including the emergency beds was the same as in the previous years, males 1,108, females 272, total 1,380.

Ever since the inception of the hospital (1925) we were not short of a bed in the female section but this section is now full and a scheme to increase the accommodation by 48 beds without prejudice to the health of the inmates is under the consideration of Government.

The appended table shows the number of patients resident in the hospital on the 1st January, 1938, and the two previous years:—

Year	Male	Female	Total
1938	1,068	256	1,324
1937	1,062	256	1,318
1936	1,053	249	1,302

It appears that the public mind in India has not yet been sufficiently educated as to the advantages of early treatment of mental diseases. During the year under review 175 patients were admitted into the hospital as so-called 'new admissions' for treatment, the majority of whom were old chronic cases for whom nothing could be done but palliative treatment with no hope of recovery. This has been our misfortune since the inception of this modern Mental Hospital which has immense facilities for the treatment of early cases.

# 6 OVALTINE'

## In Nervous States

A STUDY of the manifestations of nervous disorders, such as neurasthenia, hysteria and the various types of neurosis, shows that there is frequently an associated impairment of the general nutrition of the patient. Conversely, it is found in practice that measures taken to improve the nutrition of the patient are generally followed by a definite amelioration of the nervous state.

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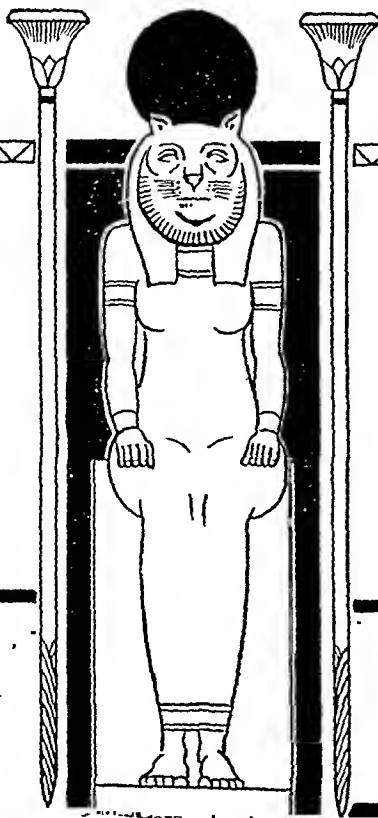
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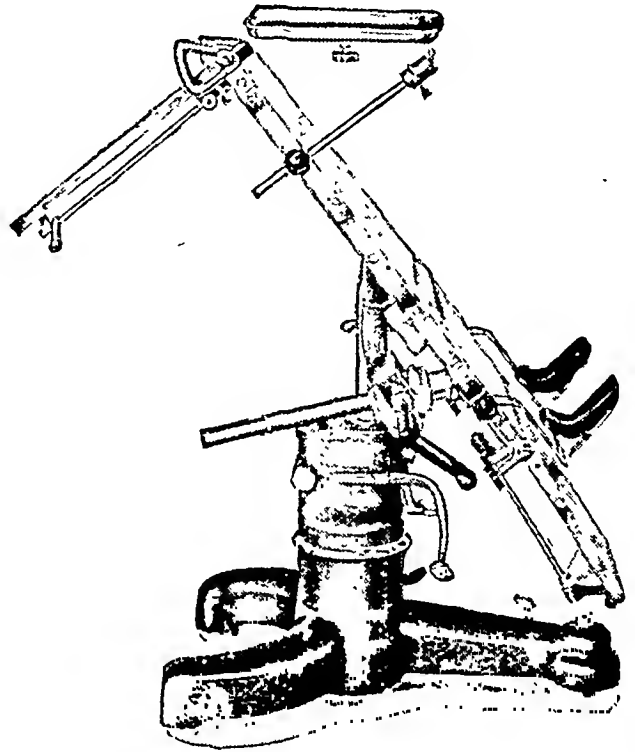
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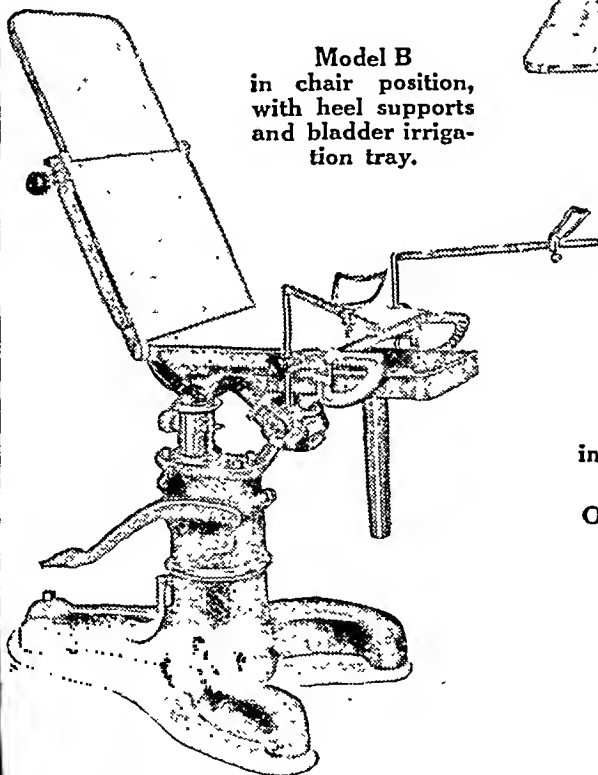
The St. Bartholomew's Hospital Operation Table is now manufactured in five different models and thus supplies a range of modern operation tables embodying the latest ideas of well-known surgeons for carrying out surgical operations.

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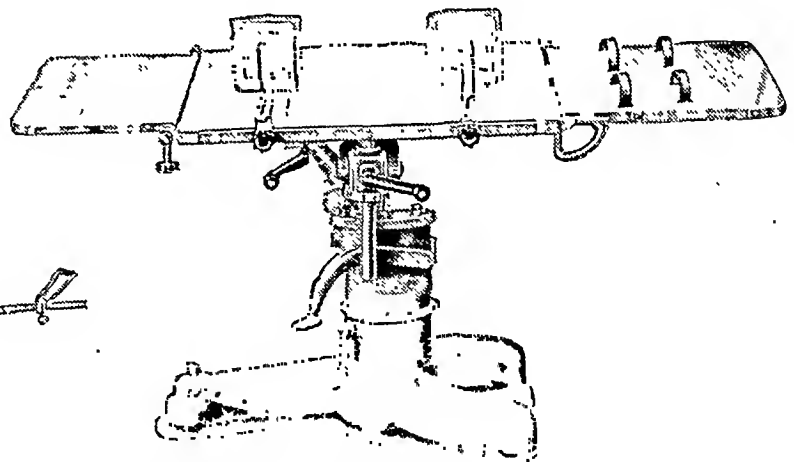


Model A

In Trendelenburg position, 55° tilt, showing shoulder rests and instrument tray in position.



Model B  
in chair position,  
with heel supports  
and bladder irriga-  
tion tray.



Model AC

in lateral position, with back elevator and lateral supports.

Over 1075 of these tables are in use at home and abroad.

*A descriptive booklet, fully illustrated, will be sent on request.*

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Mental disease is as curable as any general disease in its early stage. Those hospitals in the west which are fortunate enough to receive early cases for treatment, achieve 70 per cent recovery. The problem of encouraging early treatment cannot be solved without securing the co-operation of the public and any measure which will conduce to this end is worthy of careful consideration. Apparently antipathy is strong on the part of the Indian public to mental disease and unless this is removed no progress in the treatment of early mental cases is possible in India.

The general health of patients was good throughout the year under report and there were no outbreaks of any kind of epidemic disease during the year.

Occupational therapy was in full swing as in the past and an average employment of 80 per cent was maintained throughout the year under review. Occupation is the sheet-anchor of our treatment and every effort is made to provide suitable occupation for our patients according to individual capacity and requirement.

Rs. 600 was spent in distributing rewards to hard-working patients over and above the daily gifts of cigarettes, tobacco and other comforts.

One hundred and sixty male and 29 female patients were given hydrotherapy during the year under report with gratifying results. The average hours of immersion per patient were 253.92 hours.

*Cardiazol*.—The following table shows the number of patients treated with this drug during the year and the results:—

Number of cases treated	Recovered	Improved	Stationary
31	10	7	14

In view of the reports of the stopping of epileptic fits by anti-rabic vaccine, we decided to adopt this form of therapy to our epileptic patients. Ten confirmed epileptics (eight males and two females) were selected for this experiment. We used anti-rabic vaccine prepared by the Pasteur Institute, Patna, Bihar. The full course of anti-rabic treatment with vaccine was given to each patient but the results were not encouraging.

#### ANNUAL REPORT OF THE LEPROSY HOSPITAL, DICHPALLI, H. E. H. NIZAM'S DOMINIONS, INDIA, FOR 1938-39

DURING the past year, 216 patients have been discharged either symptom-free, or with the disease stationary and non-infective, as the result of treatment. Twenty years ago, such a statement would have been met with incredulity.

In the majority of cases, the patient can be sent home in good health and no longer a danger to others; and in some cases, if the treatment is begun in the early stages, every sign and symptom of the disease can be eradicated, as is shown by the fact that last year, 27 of our patients were discharged 'symptom free'. This emphasizes the tremendous importance of early diagnosis and treatment.

There is, however, another less satisfactory aspect; during the year 791 patients applying for admission had to be refused. Of these, many would have derived benefit from hospital treatment, but owing to lack of accommodation they had to be sent away.

The general policy of the institution remains the same with regard to admissions and methods of treatment. From over a thousand applicants every year, those most suitable for treatment or most dangerous to the community are selected for admission; the majority of the cases thus selected are either infectious cutaneous cases, or moderately early neural cases (which usually respond well to treatment, but if untreated may progress to a more advanced and infective stage). The patients whom we cannot admit are referred to the nearest treatment centre to their own homes, so that they can take treatment as out-patients, and remain under medical supervision. This system, we are convinced, is of tremendous value, for only in this way can treatment be made available for the

thousands of lepers throughout the State; and we would like to thank all those members of the medical missions, who, by helping in this way, are making a most valuable contribution to the leprosy problem and the health of the State.

#### THIRTEENTH ANNUAL REPORT OF THE RAMAKRISHNA MATH CHARITABLE DISPENSARY, BRODIES ROAD, MYLAPORE, MADRAS, FOR THE YEAR 1939

AMONG the centres of the order, the *Math* at Madras, now in existence for over 40 years, is a very influential one. As a side-activity of the *Math* the dispensary sprang up fourteen years ago. It was started in 1925 when Rao Sahib Dr. B. Raghavendra Rao, Retired Civil Surgeon of Madras, placed his voluntary service at the disposal of the institution, and undertook to meet the recurring expenditure required for the work. The devoted and self-sacrificing services of Dr. G. S. Katre, of the late Dr. S. Krishnamoorthy Iyer, and of Dr. B. Seshagiri Rao, in subsequent years, together with the substantial assistance of the members of the *Math* have enabled the institution to grow into a highly servicable centre of medical relief in the city of Madras. During the first two years of its existence the total number of patients treated was only 14,523 whereas the last two years show the number to be 168,335, which clearly shows that there has been rapid progress in its service.

## Correspondence

### VITEX PEDUNCULARIS IN THE TREATMENT OF BLACKWATER FEVER

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I read with interest Dr. Measham's article on '*Vitex peduncularis* in the Treatment of Blackwater Fever' appearing in the January 1940 issue of the *Indian Medical Gazette*. Indeed, there exists a common belief amongst the tea planters that *Vitex peduncularis* is a cure for blackwater fever, and it is for this reason that the plant is being cultivated in numerous tea estates and forest nurseries.

During recent years, the writer had a chance to observe closely not less than 20 cases of blackwater fever in Darjeeling-Terai, and has tried fresh decoction of the leaves of *Vitex peduncularis* in several of them. Owing to the fame it enjoys as a cure for blackwater fever, usually the patient's relatives procure the leaves from the neighbouring forest nursery and produce it before the physician to make a trial of it. From the few cases on which the drug was applied, it appears to the present writer that it does not possess any curative effect against malarial infection, nor does it control the temperature; but a fresh decoction of the leaves induces diuresis and thus often forms an adjunct to the treatment, as it helps to eliminate the hæmoglobin with the urine, and, once the hæmoglobin is controlled by other measures, the urine is cleared quickly. As a matter of fact, no doctor in this locality depends upon it for a cure, and aetbrin, by one or other routes, forms the routine treatment.

The drug has possibly acquired its reputation in simple cases of hæmoglobinuria where no specific treatment is needed. Moreover, in cases with associated vomiting, the decoction is not retained well, and our experience differs from Dr. Measham's in this respect also.

Yours, etc.,

J. C. BHATTACHARJEE, L.M.P.

CENTRAL HOSPITAL,  
DARJEELING HIMALAYAN RAILWAY,  
TINDHARIA,  
10th March, 1940.

## Service Notes

### APPOINTMENTS AND TRANSFERS

COLONEL R. SWEET, D.S.O., to be A. D. M. S., Lucknow District. Dated 29th January, 1940.

Lieutenant-Colonel P. F. A. Grant, O.B.E., to be Officiating O. C., C. I. M. H., Dehra Dun. Dated 11th January, 1940.

Lieutenant-Colonel K. S. Master, M.C., to be O. C., I. M. H., Peshawar. Dated 29th January, 1940.

Lieutenant-Colonel M. P. Atkinson, an Agency Surgeon, is appointed as an Additional Medical Officer at the Lady Willingdon Hospital, Lahore, with effect from the forenoon of the 14th November, 1939, and until further orders.

Major R. N. Bhandari has, on return from leave, been posted as Superintendent, District and Central Jails, Agra.

On transfer from Sargodha Major J. J. Beausang assumed charge of the office of Civil Surgeon, Gujrat, on the 16th February, 1940.

Major A. E. Kingston, on being recalled to duty, assumed charge of special duty at the Dufferin Hospital, Rangoon, on the forenoon of the 18th February, 1940.

Captain S. W. Allinson, Civil Surgeon, Bassein, on being transferred to the Military Department, made over and Major R. McRobert received charge of the duties of the Civil Surgeon, Bassein, on the afternoon of the 31st January, 1940.

Captain C. J. H. Brink is transferred to the Civil Branch of the Indian Medical Service, and that officer is appointed as a leave reserve officer against the Central Indian Medical Service cadre, with effect from the 3rd February, 1940, and is posted as Special Famine Medical Officer in Ajmer.

Captain D. K. L. Lindsay, Staff Surgeon, Detention Hospital, Rangoon, reverted to the Civil Medical Department on the forenoon of the 3rd February, 1940. He assumed charge of the duties of the Civil Surgeon, Lashio, N.S.S., on the afternoon of the 8th February, 1940.

Captain G. E. S. Stewart was transferred to Civil employment in Madras, on 16th January, 1940.

On transfer from Gujrat Captain F. V. Stonham assumed charge of the office of Civil Surgeon, Sargodha, on the 20th February, 1940.

### PROMOTIONS

#### *Lieutenant-Colonels to be Colonels*

P. B. Bharucha, D.S.O., O.B.E. Dated 6th October, 1939, with seniority from 30th July, 1933.

R. H. Candy, C.I.E. Dated 8th November, 1939, with seniority from 27th July, 1934.

W. C. Paton, M.C. Dated 10th November, 1939, with seniority from 27th January, 1935.

#### *Major to be Lieutenant-Colonel*

R. N. Bhandari. Dated 25th February, 1940.

#### *Captain to be Major*

A. B. Guild. Dated 4th February, 1940.

### RETIREMENTS

Major-General E. W. C. Bradfield, C.I.E., O.B.E., retired 8th November, 1939.

Colonel W. E. R. Williams, O.B.E., K.H.S., retired. Dated 29th January, 1940.

Lieutenant-Colonel G. F. Graham, I.M.S. (retired), was released from service. Dated 11th January, 1940.

## Note

### A PAINLESS INTRAMUSCULAR ARSENICAL IN YAWS AND SYPHILIS

INTRAVENOUS injection of neo-arsphenamine products is impracticable in some cases of yaws, syphilis and other conditions requiring arsenic therapy. On such occasions, Acetylarsan, a pentavalent organic compound of arsenic, provides a valuable alternative treatment.

Acetylarsan, injected intramuscularly, is almost painless, an advantage which should commend it especially to medical officers in outlying districts, who may be obliged to delegate a part of their work to unqualified assistants. In primary syphilis it has given results equal to those obtained with neo-arsphenamine, and there are numerous instances of cases, resistant to other forms of treatment, which have yielded readily to Acetylarsan.

A book providing comprehensive data on the indications, administration and dosage of Acetylarsan has recently been published, and will, we understand, be sent free to any medical practitioner on request to Messrs. May & Baker (India), Ltd., 11, Clive Street, Calcutta, India.

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## Original Articles

### RÔLE OF OBLIQUE OSTEOTOMY OF UPPER END OF FEMUR IN HIP JOINT SURGERY

By M. G. KINI, M.C., M.B., M.Ch. (Orth.), F.R.C.S.D.  
Surgeon, King George Hospital, Vizagapatam  
(S. India)

THE problem of derangement of the hip joint as a result of congenital, traumatic and pathological causes, with or without dislocation, is a serious one.

Any alteration in the axis of weight-bearing through the hip joint leads to disability affecting both locomotion and stability. From a study of the normal weight-bearing, it becomes clear that the weight of the body is transmitted through the sacro-iliac joint on to the head of the femur and thence along the shaft of the femur to the lower leg. In the orthograde position, stability is given to the hip joint by the pelvi-femoral and the pelvi-trochanteric group of muscles. These muscles act satisfactorily, if the *point d'appui* is satisfactory. Any alteration in this point of support affects the muscles which support the hip joint and must result in mechanical disadvantage. This is evident in cases of dislocation due to congenital, pathological, or traumatic causes, and also in cases where the neck of the femur is fractured or altered as in the case of coxa vara, or in the peculiar type of infective arthritis of infants where the head and neck become absorbed. The consequent disabilities are peculiar to each type of condition, viz, the mechanical disadvantage of the pelvi-trochanteric group of muscles which follows, as a result of alteration in the point of support.

Congenital dislocations of the hip joint are not common in South India. From a study of a large number of hip conditions in infants, it is found to be remarkably rare. In this condition the child's stability is impaired by the want of a fulcrum, as a result of the displaced position of the head, with the associated changes in head, neck, acetabulum, and muscular support. In old-standing dislocations, changes occur in the head, acetabulum, and the muscles, altering the line of pull of these muscles. It is more serious in cases of pathological conditions where, added to the acute inflammation, there is an added dislocation. This type of dislocation occurs in children between the ages of 6 and 8 years, who are usually brought to hospital with well-established deformity. The involvement of the joint supervenes on some intercurrent infection, such as pneumonia, dysentery or typhoid fever, when after a slight accident the child develops high fever with pain and swelling, resulting in an abscess which is drained outside. In my series the cause of the infection has been typhoid fever in one, dislocation in a student aged 20 years,

and smallpox in four cases. In the case of smallpox, the infection usually starts during the pustular stage, as a focus at the metaphyseal end of the bone, and when the metaphysis is intracapsular, as in the case of the hip, infective arthritis naturally follows.

One case of acute suppurative arthritis associated with jaundice and pathological dislocation due to tonsillar infection was admitted, and on examination was found to suffer from right heart failure. The child was transferred to the medical side where he died.

In old ununited fractures of neck of femur, similar problems confront the surgeon. In this case the disability is due to the break in the continuity of the point of support, and the mechanical disability that results is almost identical with that met with in an unreduced dislocation though the deformity is not so severe. Sixty per cent of these cases are poor risks on account of diabetes, renal disease, and myocarditis. One other peculiar condition deserves special mention. Several children in South India early in their infancy develop an infection of the hip joint with formation of an abscess, which points in the thigh, and after drainage of the abscess the child's condition improves. But the assumption of the erect posture and locomotion is remarkably delayed, and when the child begins to walk the gait is peculiar, resembling a congenital dislocation of the hip for which it is often mistaken. A study of a large number of such cases has convinced the author that the infection of the hip joint is due to a low-grade staphylococcus. In two cases the epiphysis of the head of the femur has been found to travel down the thigh with the abscess, as a sequestrum. A follow-up of these cases shows a gradual absorption of the head and the neck with displacement of the trochanter on to the dorsum ilii, resulting in considerable shortening of the limb. Sixteen such cases are on record and only three cases consented to submit to operative treatment. Infective arthritis or osteo-arthritis of adults are associated with pain disability and diminution in range of movement of the hip. As a result of changes which occur in the acetabulum, in the head of the femur, and in certain cases in the neck of the femur, the point of support is altered. Normally almost half of the articular surface of the head of the femur is in contact with the socket at any angle, and if this relationship is altered by the widening and the irregularity of the head of the femur, or alteration in the angle of the neck, more pressure will be borne on a restricted area with consequent alterations of the acetabulum and the head, and the development of osteo-arthritis in the joint.

The treatment of these conditions is a real problem and the aim of the treatment must be the restoration of the stability of the hip joint and if possible of its movements also. Various operations have been devised to overcome the disabilities that arise from the above-mentioned

conditions. Reconstruction of hip joint in cases of old fractures of neck of femur, arthroplasty of the hip joint, pseudo-arthrosis or arthrodesis of the hip joint in cases of osteo-arthritis or infective arthritis, with several modifications, have been devised to improve the functional range and stability of the hip joint. None of the above-mentioned operations can be universally employed in all conditions of hip joint disabilities. Each operation has its own limited scope of usefulness. There is another factor that has to be seriously considered, apart from the technical skill of the surgeon employing these different methods, *viz.* the physical condition of the patient to withstand any very severe operation. It is more important to consider this aspect in South India, where the standard of resistance of the individual is low because of the lack of dietary essentials necessary to build up the reserve to withstand any serious surgical interference.

Lorenz bifurcation which was devised by Lorenz in 1919 for the treatment of the old unreduced congenital dislocations of the hip is a simple but effective method of treatment, and can be applied with modifications in all cases where stability of the hip is desired. The object of this operation is to provide a proper support to the pelvis so that the pelvi-trochanteric group of muscles can work at a mechanical advantage. It has been the experience of the author, where this operation was done in a variety of cases, that it not only provided a support for the pelvis but also improved the range of movement. This became evident after the follow-up of these cases, the pictures illustrate the usefulness of this operation.

The principle of this operation is to do an oblique osteotomy in such a way as to get the proximal end of the distal fragment towards the lower margin of the acetabular rim and allow the upper fragment to slide down so as to make the two fragments unite at an angle serving a double purpose: (1) affording the proper *point d'appui* for the pelvi-trochanteric group of muscles to act; (2) giving a lower insertion to the glutei (part of pelvi-trochanteric group) so that they can work at greater advantage. If this point in the technique of operation is not observed, the result will be unsatisfactory. This operation has been employed in one case of congenital dislocation (?—doubtful history). The parents of the child gave a history of a fall so slight that it was unlikely that the fall caused the dislocation. There were no inflammatory changes around the joint. The gait and shortening and the clinical symptoms were those of a long-standing dislocation. Hence this case is classified as a congenital dislocation. (It is often the experience when parents bring children they give very short duration just to impress upon the doctor the acuteness of the condition with the hope that it will be easily cured.) Oblique osteotomy was also done in seven cases of old ununited fractures of neck of femur, in

two cases of pathological dislocations of the hip, in three cases of osteo-arthritis of the hip

without dislocation and in three cases of late deformities resulting from Smith's arthritis of infants. In congenital dislocation (case 16) and Smith's arthritis of infants (cases 13, 14 and 15) the stability and the movements improve even though there is marked shortening.

The Trendelenburg test becomes negative after the operation with improvement in gait (see figures A1, A2, A3 and A4).

In old ununited fractures of the neck of femur (cases 1 to 7), patients who complained of great pain and inability to walk long distances, with limited and painful movement of the hip joint

before operation, improved remarkably after operation (see figures B1, B2, B3 and B4). There is, however, a definite slight shortening. In

Case 14.

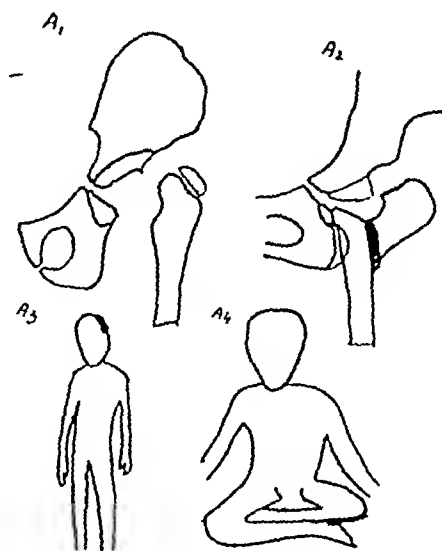


Fig. A1 is a tracing of the radiographic picture showing a dislocation of the hip with absorption of head and part of the neck of the femur, an example of Smith's arthritis of infants showing the late effects.

Fig. A2 is a tracing of the radiographic picture showing the position of the fragments after union after an oblique osteotomy.

Figs. A3 and A4 are the tracings of the clinical photographs taken one year after the operation showing the range of movement that was possible after the operation. Note the tailor's position that could be easily obtained after the oblique osteotomy.

(cases 1 to 7), patients who complained of great pain and inability to walk long distances, with limited and painful movement of the hip joint

Case 6.

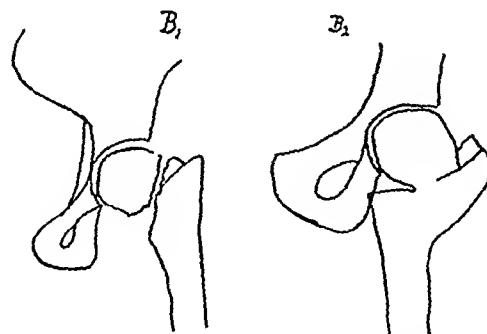


Fig. B1 is a tracing of the radiographic picture showing an old ununited fracture of the cervical part of the neck of the femur.

Fig. B2 is a tracing of the radiographic picture showing the position of the fragments after fusion after an oblique osteotomy. Note the fusion of the neck with the trochanter.

before operation, improved remarkably after operation (see figures B1, B2, B3 and B4). There is, however, a definite slight shortening. In

osteo-arthritis (cases 10, 11, 12) the pain which is great, associated with development of osteophytic growths, as shown by x-rays, greatly

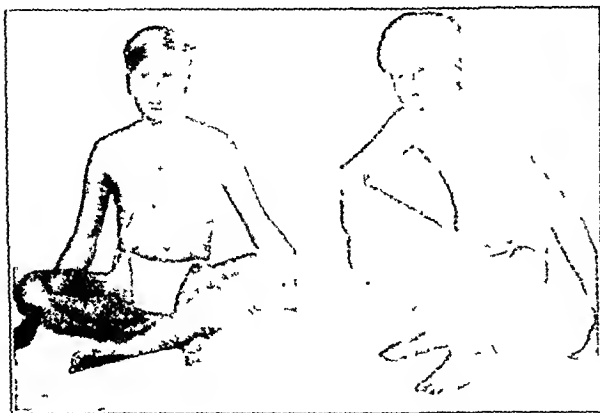


Fig. B3.

Fig. B4.

Figs. B3 and B4 show the range of movement at the hip, result of this operation.

improve in their physical well-being, gait, stability, and movement after this operation with absorption of osteophytic growths (see figures D1, D2, D3 and D4). In pathological dislocations (cases 8 and 9), which are so common in children

Case 8.

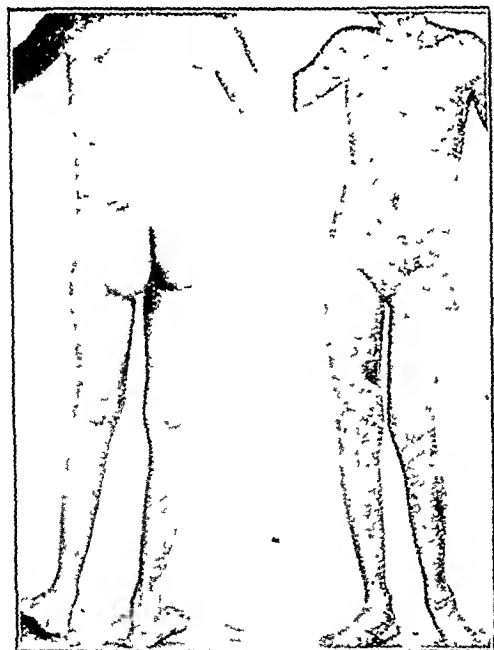


Fig. C1.

Fig. C2.

Figs. C1 and C2 are the two clinical photographs showing the condition of the hip joint.

in India as a result of varied intercurrent infections, this operation, where it has been employed, has given entire satisfaction (see figures C1, C2, C3, C4 and C5).

This operation is simple and quick in its execution with very little shock to the patient and the results that are shown by the figures in this paper indicate the scope and usefulness of this operation in hip joint surgery. Fusion of the

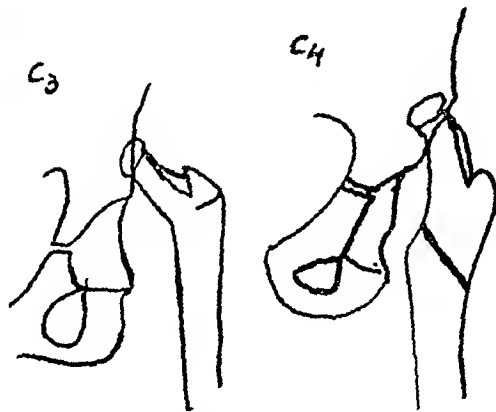


Fig. C3 is a tracing of the radiographic picture showing the pathological dislocation of the hip with osteophytic changes.

Fig. C4 is a tracing of the radiographic picture showing the position of the fragments after union after an oblique osteotomy.

hip joint has a limited scope and the results of arthroplasty are not so encouraging because the best result the author has seen in arthroplasty is a fixed hip joint. Indians who are in the habit



Fig. C5.

Fig. C5 is the clinical photograph taken one year after operation showing the range of movement at the hip.

of sitting on the floor in the usual tailor's position do not tolerate a fixed hip. Most of the poorer classes feel it a great hardship to have a fixed hip.

The follow-up of cases of oblique osteotomy has convinced the author about the usefulness

*Statement showing the type of conditions where Lorenz bifurcation was employed and the results*

Serial number	Sex and age	Occupation	Condition before operation	Result after operation
1	F., 50	..	A real shortening of $\frac{3}{4}$ inch with ununited old fracture neck of femur. Duration 4 months.	Not known. At the time of discharge firm union with a real shortening of 1 inch. Operation in 1931.
2	M., 64	Pensioner	A real shortening of $1\frac{1}{2}$ inches, result of old ununited fracture neck of femur. Duration 4 months.	A real shortening of $1\frac{1}{2}$ inches. Good movements at the hip. Patient can squat on the floor in tailor's fashion and can walk long distances. Followed for 6 years. Operation in 1932.
3	F., 40	..	A real shortening of $\frac{1}{2}$ inch due to an old ununited fracture neck of femur. Duration 6 months.	Not known.
4	F., 50	..	A real shortening of 1 inch, result of old ununited fracture of the neck of the femur. Duration 4 months.	A real shortening of $1\frac{1}{2}$ inches. Patient's stability and movements good. Has been followed for 3 years.
5	M., 40	Sanyasi	A real shortening of $1\frac{1}{2}$ inches, result of old ununited fracture of neck of femur of 7 years' duration.	Stability and gait and movements at the hip very good; can sit in tailor's fashion.
6	M., 25	Tailor	A real shortening of 1 inch, result of old ununited fracture of neck of femur of 6 months' duration.	A real shortening of $1\frac{1}{2}$ inches. Movements at the hip very good. Has been followed for 2 years. Figures B1, B2, B3 and B4.
7	M., 50	Coolie	A real shortening of 1 inch, result of old ununited fracture of neck of femur of 6 months' duration.	Done in 1938. Result is being watched.
8	F., 9	..	Pathological dislocation of the hip due to infective arthritis with a real shortening of 1 inch, duration 1 year.	A real shortening of $1\frac{1}{2}$ inches compensated by a raised sole. Movements at the hip satisfactory. Case done in 1937. Progress satisfactory. Figures C1, C2, C3, C4 and C5.
9	F., 7	..	Pathological dislocation of left hip with a real shortening of $1\frac{1}{2}$ inches. Duration 6 months.	Done in 1938. The child's movements at the hip were remarkably good after the operation before discharge.
10	M., 14	Student	Arthritis of the hip without dislocation with marked adduction deformity and $\frac{1}{4}$ inch shortening. Duration 1 year.	Very good range of hip movements. Patient can squat in Indian style without pain and has been followed for 6 years.
11	M., 30	Agriculturist	Osteo-arthritis of the hip with marked pain and limitation of movements. Duration 3 months.	Very good. No pain. Range of movements has increased and is able to do agriculturist's work. Followed for 5 years. Figures D1, D2, D3 and D4.
12	M., 25	Coolie	Arthritis of hip with marked flexion deformity at the hip. Duration 1 year.	Range of movements definitely improved. Patient is able to sit and bend his hip though he cannot sit in tailor's fashion.
13	M., 11	Student	Arthritis of infants early in life with absorption of head and neck of femur. A real shortening of $2\frac{1}{2}$ inches since childhood.	Range of movements definitely improved. The tired feeling the boy used to have before operation disappeared and he can run and kick a football. Real shortening is 3 inches which was compensated by a raised sole of the boot. Followed for 6 years.
14	M., 8	Student	Arthritis of infants resulting in absorption of head and neck of femur with a real shortening of $1\frac{1}{2}$ inches since childhood.	Very good movements at the hip, marked stability, no pain, can run and kick a football. A real shortening of 2 inches which was compensated by a raised sole on the shoe. Followed for 5 years. Figures A1, A2, A3 and A4.
15	M., 26	Beggar	Arthritis of infants with marked shortening of 2 inches since childhood.	Stability and movements markedly improved. Patient able to squat in Indian fashion. Followed for 2 years. Good at time of discharge.
16	M., 5	Student	Dislocation of hip. Difficult to say whether it is congenital or traumatic. Three closed reductions were tried before operation without any success. Lorenz bifurcation was done.	Result is being watched. No reply has been received to the letter written. Done in 1937.



of this operation with regard to the convenience which it affords to the common Indian patient in his normal daily habits, apart from the stability of the hip, and hence it is advocated.

Case 11.

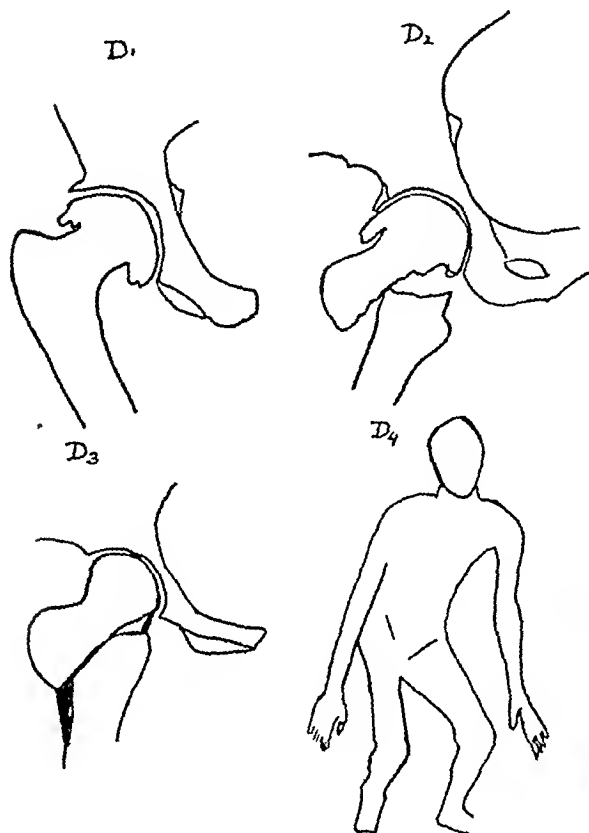


Fig. D1 is a tracing of the radiographic picture of the hip joint showing changes in the head, acetabulum, neck with formation of osteophytes on the acetabular rim and around the head of the femur.

Fig. D2 is a tracing of the radiographic picture showing the position of the fragments after an oblique osteotomy.

Fig. D3 is a tracing of the radiographic picture taken 6 months after operation showing the fusion of the fragments after an osteotomy, and note the disappearance of the osteophytes from the head of the femur and the acetabular margin.

Fig. D4 is a tracing of the clinical picture taken before discharge from hospital. Note the range of movement that was possible at the time of discharge. He subsequently has written saying that his range of movement has considerably increased and he can squat down though not actually able to assume a tailor's position while sitting.

My grateful thanks are due to Mr. T. P. McMurray, Director of Orthopaedics, Liverpool University, who gave the author of this article an insight into the usefulness of this operation, while a post-graduate student in Orthopaedics in Liverpool. My grateful thanks are also due to Dr. P. Kesavaswami, the Radiologist of King George Hospital, for his help in the reproduction of the photographs.

(Continued at foot of next column)

## AN OUTBREAK OF EPIDEMIC DROPSY

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CHOPRA *et al.* (1939) showed, by a controlled feeding experiment in man, that argemone oil (expressed from the seeds of a weed *Argemone mexicana*) produces symptoms resembling those of epidemic dropsy. In this experiment five individuals, who ate food cooked in mustard oil containing known quantities of argemone oil, developed well-marked oedema and two of them showed the characteristic flushed appearance of the skin and had cardiac involvement (dilatation and murmur). It is interesting to recall that Sarkar (1926) first implicated argemone oil in an outbreak of epidemic dropsy in Malda district. Kamath (1928) described an outbreak in Ganjam district in which oil pressed from certain seeds (locally known as 'odissimari' seeds) was popularly believed to be responsible for the outbreaks of the disease. Samples of 'odissimari' seeds were obtained and identified as the seeds of *Argemone mexicana*. Kamath, in discussing the various theories, wrote 'Another idea gaining ground among the villagers is that the disease is due to some poison in adulterated "gingelly" oil. They allege that "gingelly" seeds are mixed with seeds of an agency plant called in Oriya "odissimari" and that the oil from the latter seeds is poisonous. In support of this theory, they state that the pure oil of these seeds when applied to the body produces erythema and local swelling, and that, if internally administered, it is certain to produce the disease. Enquiries made from those who extract the oil bear out this statement'. It is unfortunate that these two reports were neglected and forgotten till the recent work of Lal and his collaborators (1939), who produced more extensive epidemiological data incriminating

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jaundice are the only signs. Their interpretation undoubtedly offers certain difficulties. Far too often a diagnosis is ready which means nothing in itself, but is satisfactory in producing a soothing effect on the patient's mind. 'Sluggish liver' is neither a scientific term, nor does it exist from a pathological point of view. The underlying condition causing the aforementioned symptoms is always a clinical entity which can and must be properly diagnosed. Amœbic infection is many times responsible but is rarely thought of in this connection, because unfortunately the term 'amœbic dysentery' has produced some confusion. Amœbiasis in its subchronic and chronic stage is accompanied in the majority of cases by constipation and not by diarrhoea. With this fact in his memory the possibility of amœbic infection should not escape the physician's attention.

On the other hand, short periods of diarrhoea under these conditions are frequently classed as acute indigestion. At a later stage they may be labelled 'colitis'. Symptomatic treatment is then induced, which may be temporarily successful in suppressing the symptoms. If they reappear, as they are bound to do, the former diagnosis seems even more justified. It is obvious what harm will be done. By simple examination of the stools the patients would have been saved from indefinite periods of physical and nervous incapacity.

Involvement of the liver due to amœbic infection was found in 32 per cent of the cases. Moderate increase in size and slight hardening and tenderness of the liver were the main symptoms. Bile pigments in the urine were found in seven cases (9.6 per cent), bilirubin in four cases (6 per cent), and the liver function test (Takata-Ara) gave positive results in 11 cases (12 per cent). The van den Bergh reaction was positive in four cases (6 per cent).

In the tropics, impairment of the liver function seems to have even more importance; here cirrhotic liver changes, especially of the atrophic type with portal cirrhosis, reach high proportions. If such causes as malaria, syphilis and chronic alcoholism can be excluded the problem arises whether or not a number of these cases may be due to the continuous damage which this organ suffers from chronic amœbic infection. Research on this line would prove very useful.

#### Treatment

As far as treatment is concerned we have emphasized that in the first place every positive case of amœbiasis should receive treatment. The choice of the drug varies with the case. Treatment is guided by the natural advice that the measures employed must not do the patient further harm. This leads necessarily to the exclusion of drugs apt to affect organs already endangered by the infection.

Some recent arsenical preparations exert decidedly ill-effects on the liver, a fact which is the more deplorable as these drugs are powerful

amœbiocides. Their use has to be limited to cases which resist other therapeutic efforts\*.

Emetine for the same reason can be used only in comparatively small doses. Higher dosage, which might result in a complete eradication of the infection, cannot be administered because of the toxicity of the drug. It has, however, an uncontested advantage over all anti-amœbic remedies in amœbic liver abscess and the rare complications affecting lungs, brain and spleen.

Searching for an anti-amœbic treatment which has no undesirable side-effects, but which is, on the other hand, at least as effective as the arsenicals or emetine, we investigated the therapeutic value of an iodochloroxyehinolin compound with addition of sapamin (Enterovioform, Ciba). Sapamin is said to increase the emulsification of the active principle. The drug has been developed because of the amœbicidal properties *in vitro* of vioform, which is used as a powder in skin lesions and surgical conditions, and has decidedly antiseptic qualities.

The first group of patients with gastro-intestinal symptoms related to infection with *Entamoeba histolytica* consisted of those with both cystic and vegetative forms in their stools, who were thus classified as suffering from acute or sub-acute amœbic dysentery. The clinical symptoms did not differ from the classical descriptions sufficiently to justify a lengthy enumeration.

After an initial saline purge, 15 patients were given two tablets of enterovioform (0.25 gramme) thrice daily, on a full stomach, for a period of ten days. Clinical symptoms disappeared after an average of three days and no amœbæ could be found in the stools after an average of five days. To three cases with diarrhoea and tenesmus (30 to 36 stools in 24 hours), enemata made of two or three tablets of enterovioform in normal saline were given in addition to the oral treatment. Almost immediate relief from the intestinal spasms was effected. The enemata were discontinued as soon as the frequency of the stools returned to a reasonable level. One case resisted this form of treatment for several days and needed large doses of opium and bismuth.

Four of the 15 patients have been observed for only 20 days after the treatment was completed. No amœbæ occurred in the stools during this time. Eleven cases were followed up to an average of six weeks and regular weekly stool examinations were made after a saline purge had been given. In no instances were amœbæ found, the longest period of observation having been four months. This result enables us to state that a complete cure was obtained.

Some patients continued to have slight epigastric pain and occasional loose stools. Gastric

\* We do not think that this can be applied to all the arsenicals used in the treatment of amœbiasis.—  
Editor, I. M. G.

analysis revealed, in all but one case, marked hypochlorhydria. Adequate treatment of this condition led to complete freedom from symptoms.

The second group of patients had only amœbic cysts in their stools but suffered from gastro-intestinal symptoms for which the parasite was held responsible. These cases represent the sub-chronic and chronic clinically active amœbiasis. Most of the patients sought admission to the hospital for other than the troubles actually connected with the amœbic infection. In many cases the routine examination of the faeces revealed the parasite as a purely accidental finding. Nevertheless, appear in this group, only patients whose gastro-intestinal symptoms were definitely due to the activity of *Entamœba histolytica*.

Enterovioform was administered in the same way as above. In an average of five days the condition cleared up and abdominal discomfort ceased. In follow-up examinations extended over an average of five weeks, 11 cases were freed from the parasite and two remained positive. In these cases emetine (1 gr. daily for ten days) was injected. One case was thereafter cured, but in the other, cysts continued to be present in the stools, although for the time being no symptoms of the infection reappeared.

Thus, enterovioform proved to be effective in 86 per cent of the cases in this group, a result which conforms to the percentage of cures seen in any other energetic and complete treatment.

The third group was that of 18 cases of amœbic infection with cysts only, without any appreciable symptoms related to the infection. The doses of enterovioform given were identical to those of the preceding groups. Sixteen cases showed afterwards no amœbæ in their stools during the period of observation of an average of four and one-half weeks after this treatment. In two cases the cysts were perhaps reduced in number, they were not found at each weekly examination, but they did not disappear completely.

As in these silent infections, the work of destroying the parasites is that of the drug alone, whilst the organism probably takes little or no part in the fight against the parasite, the result of the treatment as shown by absence of amœbæ, even over a prolonged period, must be critically interpreted, because amœbæ may not show themselves for a considerable time. The absence of amœbæ in 83 per cent of the patients after a ten days' course of enterovioform is nevertheless a very satisfactory result.

For practical purposes, in order to obtain quicker and safer results, one may give in chronic asymptomatic amœbiasis a combined treatment of emetine and enterovioform. It has the advantage of shortening the course of treatment. Six daily injections of emetine (1 gr.), together with two tablets of enterovioform, thrice daily, over the same period have permanently

freed eight patients suffering from chronic amœbiasis from recurrence of the parasite in the stools. Neither of these drugs alone would be sufficient to yield a cure and it must be supposed that they each complete the action of the other.

#### *Symptomatic treatment*

In testing enterovioform we gave the drug to a number of patients not suffering from amœbic infection in which symptoms such as diarrhoea, intestinal spasms and similar conditions were caused by different infections. We did not expect a cure, but at least a symptomatic relief.

Enterovioform proved to be anti-fermentative and anti-putrefactive in a small number of dyspeptic disorders. It relieved the tenesmus in enterocolitis to a great extent, especially if given in the form of an enema. In bacillary dysentery we gave enterovioform because it acted favourably on the common bacterial flora, preventing an increase of their virulence. However the total of these cases is as yet too small to be summed up statistically.

We feel that colitis is a definite indication for enterovioform treatment but it must not be used exclusively. The aetiology of colitis is not yet clear, and relapses may occur if the treatment is only directed against its symptoms, which often disappear with enterovioform. In recurrent colitis every effort must be made to detect the real cause. Symptomatic treatment as a rule is the last resource in recurrent intestinal disturbances.

#### *Comment*

The frequency of amœbiasis constitutes a definite therapeutic problem and is not only confined to the cases in which the disease manifests itself with the classical symptoms; equally important is the asymptomatic and clinically silent infection. We have seen in our hospital many cases of different diseases, such as tuberculosis of the lungs, anæmias of different origin, and asthma with co-existent amœbic infections. After the above-outlined anti-amœbic treatment, these cases were followed rapidly by marked improvement of the patients' condition, previously not influenced by the original treatment.

There is no innocuous amœbiasis and no such thing as a 'healthy carrier'.

The possible consequences of long-standing infections with *Entamœba histolytica*, on the organism as a whole and on the liver in particular, are emphasized by the large number with hepatic dysfunction and demand that every case be adequately treated.

Treatment has to be planned in a way that exterminates the infection and does not harm the patient. Arsenical preparations are contra-indicated except when other treatment fails. Emetine is the drug of choice in amœbic abscess of liver, lungs, brain and spleen. In all other conditions less toxic preparations are preferable.

Enterovioform (Ciba) has shown its ability to deal successfully with acute, sub-acute, chronic and sub-chronic infections. It is particularly useful in cases in which the whole process suggests a marked activity of the parasite, when although diarrhoea may be absent, the parasite action is shown only by the stool examination, mucus, blood, pus cells, and undigested food being found. Such cases are best classified as 'sub-chronic amœbiasis'.

Under these conditions a cure may be expected in 85 per cent of all cases, after a ten days' course of enterovioform (Ciba), two tablets (0.25 gm.) thrice daily.

In chronic infections of long standing, with or without clinical symptoms, a combined treatment of enterovioform and emetine for six days may be given.

No after- or side-effects have been observed with enterovioform, and no symptoms of iodism, even in susceptible patients in which other iodine compounds (potassium iodide) caused marked symptoms.

No incompatibility with any other kind of pharmaceutical preparations has been detected.

It is essential that check-up examinations of the stools be done one week after the treatment and again after three or four weeks, otherwise cases which resist the treatment will not be detected\*.

#### Summary

The incidence of amœbic infection in unselected patients composed almost equally of rural and urban elements was 23.2 per cent.

Of the infected cases, 30 per cent showed in one way or the other symptoms of acute or sub-acute processes.

In 32 per cent of the infections pathologic conditions of the liver, excluding liver abscess, were found.

Enterovioform (Ciba) produced a cure in all cases of acute amœbic dysentery (15 cases), in 86 per cent of sub-chronic infections (11 of 13 patients) and in 83 per cent of chronic amœbiasis (16 of 18 patients), when given for ten days in a dose of two tablets (0.25 gm.) thrice daily, after meals.

The period of observation after the treatment was such as to allow definite conclusions.

Combined treatment by enterovioform and emetine over a period of six days is sufficient to deal with chronic asymptomatic amœbiasis.

The author is indebted to Dr. R. J. Weingarten, M.D., P.M.O., Bikaner State, for his assistance and kindness in allowing data of this paper to be collected from this hospital, and also to Dr. S. D. Sahasrabudhe, M.B.B.S., Pathologist, for his assistance in connection with the laboratory work.

\* Few workers on the treatment of amœbiasis have provided statistically acceptable evidence of cure in the cases they report. To start treatment after a single observation of cysts in the stools and to proclaim a

(Continued at foot of next column)

## QUININE AND ATEBRIN IN THE CONTROL OF MALARIA; WITH SPECIAL EMPHASIS ON THE PRACTICAL AND ECONOMIC VIEWPOINTS

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### 1. Object of the experiment

THE primary object in administering the course of drugs prophylactically, as outlined in this paper, was to determine the method by which a given sum of money could be expended to give the greatest possible reduction in malaria incidence in a tea estate population at a definite period of the year—namely, when the demand for labour was at its greatest.

With this object in view as the primary consideration, the method was so arranged as to give as much information as possible as to the relative value of prophylactic administration of quinine and atebrian in reducing the incidence of malaria in this population.

### 2. Data regarding the incidence of malaria on the estate

The estate chosen was Towkok, one of the Assam Company's gardens in the Sibsagar District of Assam. The population on the estate is resident in several groups. The largest group comprises 2,173 persons who are quartered in a clearing of 75 acres which is surrounded on three sides by tea land, and one side by grazing land and light jungle. These lines are known as the 'main lines'. There are three other groups of coolie lines situated some miles away, the largest of them being known as 'Namtolla lines' which are situated three miles distant on the boundary of the estate outside the tea land. The resident population here is 750 persons, and they live in a scattered village extending over some 260 acres.

Towkok estate has for many years had a notoriously high sick rate and malaria has been hyperendemic. In 1934, temporary biological control measures were instituted in the half mile circle surrounding the main line.

The expenditure on larvicides and sprayers was as follows:—

1934	..	Rs. 911
1935	..	Rs. 1,019
1936	..	Rs. 1,092
1937	..	Rs. 1,443

The average annual cost including labour was about Rs. 1,400.

The terrain is of a hilly nature; areas of high land, on which tea is grown, are separated

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cure after four consecutive negative findings is not sound. Unless there is evidence that cysts were consistently present before treatment a dozen negative examinations scarcely indicate even a reduction of the infection.—EDITOR, I. M. G.

by a network of *hullahs* and natural streams. It is difficult—if not impossible—to improve the drainage. *Anopheles minimus* is the most important vector and can be found breeding in over ten miles of *hullahs*, drains and streams within the half mile circle surrounding the main lines. Many of these areas could be shaded only by tall shade vegetation, such as bamboo, but the policy of the management has been to clear bamboo from the edges of *hullahs*, as it gave an undesirable degree of shade and humidity to the neighbouring tea bushes, and furthermore it was considered that pests and blights spread from it into the tea.

The terrain is very similar at the Nantolla line but in addition to malariogenic *hullahs* there are two large perennial streams winding through the village.

Figure 1 shows the average daily number per thousand of the labour force off work month by month, 1932–37, due to malaria and to sickness from all causes on the whole estate. From this it can be seen that the incidence of sickness from all causes and from malaria is low from November to May and high from June to October, the highest peak generally being in June and July, while a second peak may occur in October.

It also demonstrates that the institution of temporary biological control methods in the half mile surrounding the main line population in 1934, was associated with a decrease in malaria on the estate. Unfortunately, previous to 1934, there are no records of the cases from each line, so it is not possible to show the malaria rate in the main line population before and after introducing biological control. The average daily malaria and total sick rates in the whole labour force in the two years prior to any control and in the four years during which larvicides were applied at the main lines are as follows :—

	AVERAGE DAILY NUMBER OFF WORK PER 1,000	
	Due to all causes of sickness	Due to malaria
Before any control, 1932–33.	47	19
During partial control, 1934–37.	42	10

Figure 2 shows the average daily number per thousand off work due to malaria from 1934–37 from the main line and the Nantolla line for

comparison and shows a slightly higher sick rate at Nantolla.

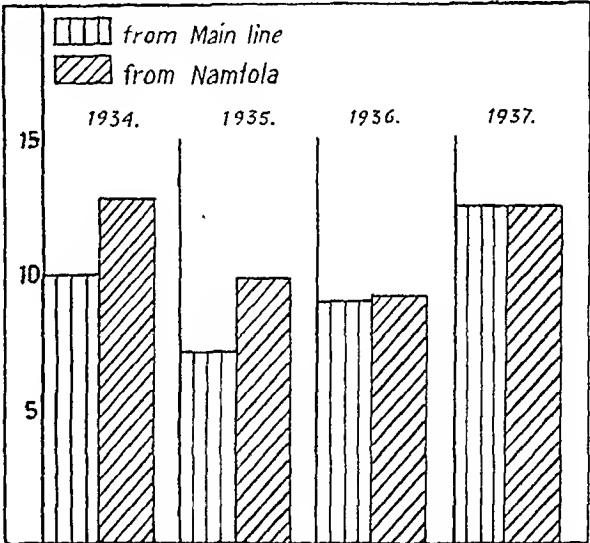
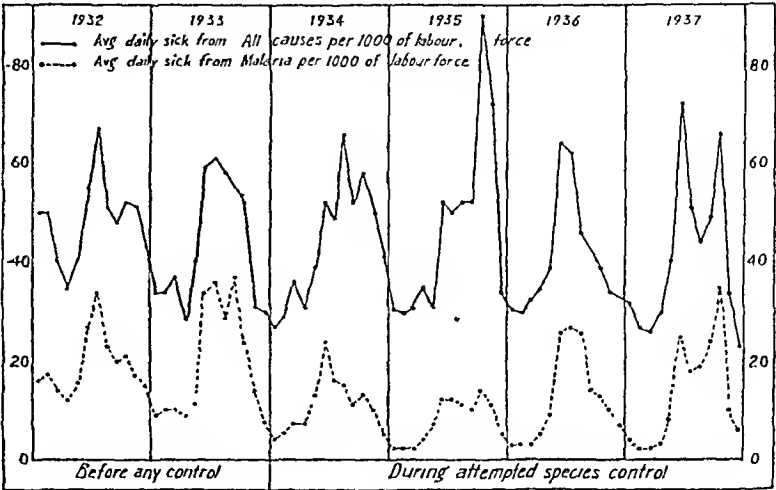


Fig. 2.—Showing average daily sick from malaria per 1,000.

The spleen rates were taken in March of 1934 and of 1938 and were as follows :—

		Main line	Nantolla line
Before any malaria control measures.	March 1934	57 (243 examined).	74 (136 examined).
After 4 years of control in main line.	March, 1938	50 (390 examined).	78 (175 examined).

Some degree of reduction was obtained as is shown by the fall in sickness and by the fall in spleen rates, but in view of the disappointing results and in view of the objections to covering the *hullahs* with shade vegetation, and the apparent impossibility of adequately controlling the breeding with an economic expenditure in



larvicides, it was decided to abandon biological control methods in 1938 and to attempt to reduce the incidence of malaria in the main line by a mass administration of drugs, limiting the expenditure to Rs. 1,400 the same sum spent, on an average, annually in the previous four years.

### 3. *The factors determining the period of treatment*

The greatest incidence of malaria, as is shown in figure 1, is generally in June and July, with sometimes a second peak in October. The period when the labour on the estate is most urgently needed is June to September, when the greatest part of the crop is made, and the maximum degree of efficiency is called for from the labour. It was, therefore, decided to start mass treatment in the middle of May and to stop it in the latter part of September.

It was appreciated that treatment would be discontinued before the risk of fresh infection was past, and that there would in all probability be a rise in the malaria incidence in October, but it was considered that the sum that had been earmarked for the treatment could be spent most economically by reducing the number and intensity of attacks between June and September. It was decided to confine treatment to the residents in the main line only and to leave the population in the Namtolla line to serve in some measure as a control.

### 4. *The factors determining the dosage selected and method of administration*

An experiment to obtain data on the relative values of atabrin and quinine under field conditions was planned, the method being very largely based on the experiment in clinical prophylaxis, carried out in Malaya by Field, Niven and Hodgkin (1937) at the invitation of the League of Nations Health Organization, but, in view of the financial considerations imposed, considerable modification was necessary and the standard of the work as a scientific experiment falls very far short of the Malayan work. Field and his collaborators had divided a population into three groups, in which all factors influencing malaria incidence were as far as possible equal. The population of Towkok main line was divided into three groups, the division being so arranged that the houses of each group were evenly distributed over the area of the lines and as far as possible the same number of children and of recently recruited coolies were drafted into each group. The castes were also, as far as possible, equally distributed between the three groups.

Field *et al.* (*loc. cit.*) in their experiment administered atabrin to one group, quinine to the second, and some neutral dummy tablets to the third, which served as a control group. The atabrin group were given by them 0.4 gramme of atabrin weekly, 0.2 gramme being administered on two successive days in each week, the quinine group were given 0.4 gramme quinine

hydrochloride, daily. Field (1937) in his preliminary paper suggested that 0.3 gramme in three tablets, might with advantage be given once weekly instead of the 0.4 gramme at two administrations; this would reduce the cost by 25 per cent and necessitate only one mass treatment weekly instead of two.

If with this modification the Malayan experiment had been repeated on Towkok and continued for the transmission season, it would have required 51,008 tablets of atabrin costing Rs. 2,791 and nearly 79 pounds of quinine, costing Rs. 2,047, a total of Rs. 4,838. Field, however, had also experimented with an adult dose of 0.2 gramme weekly and had reported that malaria 'continued amongst the adults with a numerical reduction in number of attacks of approximately 75 per cent as compared with the control'.

On these results it was considered that with a limited quantity of drugs a greater reduction in incidence and intensity of malaria attacks could be expected by administering the dose of 0.2 gramme weekly to adults and a proportionately reduced dose to children, than by administering 0.3 gramme or 0.4 gramme weekly to a smaller proportion of the population.

#### *Dosage selected*

To group A atabrin was given as follows:—

The course commenced with a 'blanket treatment' for five consecutive days.

Adults (over 12 years)	were given	0.2 gramme daily.
Children 5 to 12 years	..	0.1 " "
Children under 5 years	..	0.05 " "

The 'blanket treatment' was to be followed by the same daily dose administered on one day in each week.

To group B it was decided to administer quinine on five consecutive days in every third week as follows:—

Adults (over 12 years) quinine bisulphate grain vi.

Children 5–12 years, quinine bisulphate grain iii.

Children under 5 years, quinine ethyl carbonate grain 1½.

The quinine bisulphate was given in solution and the quinine ethyl carbonate for the young children was given in milk.

This method of giving quinine for prophylaxis was chosen as in previously conducted field experiments I had satisfied myself that it was a practical method of economically reducing the number and intensity of attacks.

For group C a dose of infusion of quassia was available on one day in each week for any person who felt aggrieved at not receiving any course of medication.

### 5. *Arrangements for administration and practical difficulties*

Certain practical difficulties in administration had to be met. The labour is almost entirely



illiterate and many of the coolies are very primitive. Whereas now-a-days there is not much difficulty in getting sick persons to attend hospitals for treatment in most tea estates in Assam, there is often considerable difficulty experienced in inducing healthy persons to attend and receive drugs for prophylactic purposes. The difficulty is accentuated at the present time in Assam, as it is the policy of the industry to abandon as far as possible any methods of coercion.

The object of the treatment was explained to the labour force, the sirdars were made responsible for seeing the coolies attended hospital on the right days. The estate manager and European staff gave every possible support to the experiment, and as often as possible a European member of the staff or myself was present at the administration.

The treatment was given at about 7 a.m., as the coolies left their houses to go to work. Some of them have tea and some a little cold rice before going to work, but many do not take food till the evening so in a number of instances the drugs were taken on an empty stomach. This was a disadvantage, but it was not considered practicable to administer the drugs after the evening meal.

There was little opposition to taking the atebtrin tablets on account of the absence of any unpleasantness either on swallowing or subsequently, and also on account of the small amount of inconvenience and delay in having the treatment on one day only in each week. A high percentage took the dose regularly.

Much more difficulty was encountered from the quinine group. The coolies disliked the delay in getting to work for five consecutive days in the week. There were a good many complaints of dizziness and nausea. On account of coolies' dislike of quinine and to avoid the risk of them holding a tablet in their cheek and subsequently ejecting it, the quinine was given in solution and this of course, although reducing one difficulty, gave rise to another, as the taste of quinine is generally strongly disliked. Very considerable trouble was involved in inducing the coolies to attend the musters regularly and although every effort was made there were a good many defections.

At each muster the medical staff worked in two teams each team consisting of one man to call and mark the register, one to measure and administer the dose and one to give a following draught of water. As some 600-700 persons had to be treated at each muster a certain amount of waiting was unavoidable.

#### 6. Method of recording

Separate registers were kept for each group, every individual's name being written in and the members of households being grouped together. The households were classified under the names of the sirdars who were responsible for them, so that the names of any absentees could readily be given to the sirdar and efforts

made to bring them subsequently for their dose. Every dose taken was marked in the register so the number of doses taken or missed by every individual could readily be obtained.

In addition, index books were kept for each group showing the names of all persons attacked with malaria, the number and date of attacks and the number of days of treatment for each attack. The diagnosis of malaria attacks rested on the clinical diagnosis made by a capable and experienced assistant medical officer. Although there is doubtless a certain degree of error, I am satisfied that the error is small, and, for representing the relative number of attacks in different groups, the error is almost negligible. The number of new coolies arriving during the course of treatment was so small that it can be ignored.

#### 7. Dates of starting and discontinuing course and numbers treated

Originally it was planned to commence the treatment in the second half of May and to discontinue in the middle of September.

The blanket treatment to group A was given in the week ending 21st May and treatment was continued once a week till the week ending 10th September. However, in view of the fact that there was every prospect of fairly extensive fresh infections in the latter part of September and furthermore as some atebtrin was in hand owing to a fraction of the group not having attended at each treatment, it was decided to have one further muster in the week ending 25th September.

The first muster for the group B was held in the week ending 28th May and musters were held in every third week until the final course, in the week ending 1st October.

*Group A.* At the 'blanket treatment' the persons taking treatment were as follows:—

Full 5 days	..	..	611 persons	83 per cent.
4 "	..	..	71 "	9 "
1-3 "	..	..	39 "	6 "
Untreated	..	..	15 "	2 "
			736 persons	

At the subsequent 17 treatments an average of 87 per cent of the group took the drug, the highest number receiving the dose at any muster being 94 per cent and the lowest at any muster being 74 per cent in one exceptionally bad week. The number of persons in the group fluctuated only very slightly, the largest number in any week being 736 and the smallest 726. The total amount of atebtrin used was  $22,673 \times 0.1$  gramme tablets.

*Group B.* The administration of quinine was done with much less co-operation from the coolies. The highest proportion of the group taking the full five days' course was 84 per cent at the first week of treatment and the lowest 24 per cent at the last week of treatment. On an average over the seven courses, 58 per cent took

the full five days and 75 per cent took four days or more, 25 per cent taking three days or less. The number of persons fluctuated only slightly, the highest number being 728 and the lowest 713. The total amount of quinine used was 73,560 grains.

The number of persons in Group C averaged 724.

### 8. Controls

It is almost impossible to arrange for perfect controls in a field experiment of this nature. The results obtained, however, by the treatment have been measured in the following ways:—

Firstly, the combined results in the main line population obtained by the exhibition of quinine and atabrin to two-thirds of the population, may be compared with the results by anti-larval measures, undertaken in the previous four years. This may be done by comparing the figures for sickness from all causes and from malaria in 1938 with the corresponding figures for 1934–37. These figures must be considered in the light of evidence regarding the relative number of malarial vectors in the 1938 transmission season and previously.

Secondly, the relationship of the malaria case rate in the Namtolla and main line populations during 1938 can be compared with the relationship of the 9 case rates in these two populations 1934–37. This again is not an altogether convincing method of estimating the value of the treatment, as, although the two populations are separated by only three miles and are subject to the same climatic conditions and a similar terrain, the conditions cannot be considered as identical.

Thirdly, the number of cases of clinical malaria may be compared in the three groups A, B and C, in the main line population in 1938. For this estimation, the control is not altogether satisfactory, as, although the risk of fresh infection must have been equal for all three groups, it must be borne in mind that there is a fallacy in assuming that the malaria rate in group C—the untreated group—represents the rate that would have been expected, if the whole population in the main line had been untreated. By administering anti-malarial drugs to two-thirds of the population the parasite rate, and with it the gametocyte rate, was reduced in the treated persons quite apart from any particular selective action of the drugs on gametocytes. The lowering of the gametocyte rate in any population must reduce the infectivity rate of the local vectors and hence reduce the risk of fresh infection in the whole community, both those who are receiving drugs and those who are not. This is supported by the fact, as will be shown later in this report, that, although there were approximately the same number of attacks of clinical malaria in each of the three groups, the incidence of clinical malaria in the population was nevertheless reduced. The fact that the infectivity rate of the local vector is reduced is much

more adequately demonstrated by Field *et al.* who report that '... the administration of prophylactic drugs ... was associated with a substantial reduction in the sources of mosquito infection'. An analysis of a table given by these authors in appendix A of their report shows that, during a period of administration of drugs to two-thirds of the population of estate T, in 707 blood examinations from the control group 16.6 per cent showed gametocytes, in 798 examinations from the quinine group 8.8 per cent showed gametocytes, and in 901 examinations from the atabrin group 1.2 per cent showed gametocytes.

### 9. Results

(a) The average daily number of persons off work per thousand of the labour force in the main line due to all causes of sickness and due to malaria from 1934–38 is shown in graphic form in figure 3. These sick rates may be summarized as follows:—

AVERAGE DAILY NUMBER OFF WORK DUE TO SICKNESS PER 1,000		
	Due to all causes	Due to malaria
1934–37 .. ..	41.5	10
1938 .. ..	29.0	6

The loss in work due to malaria in 1938 was substantially lower than in the previous four years when larvicidal methods had been used to control malaria. The figures of sick from all

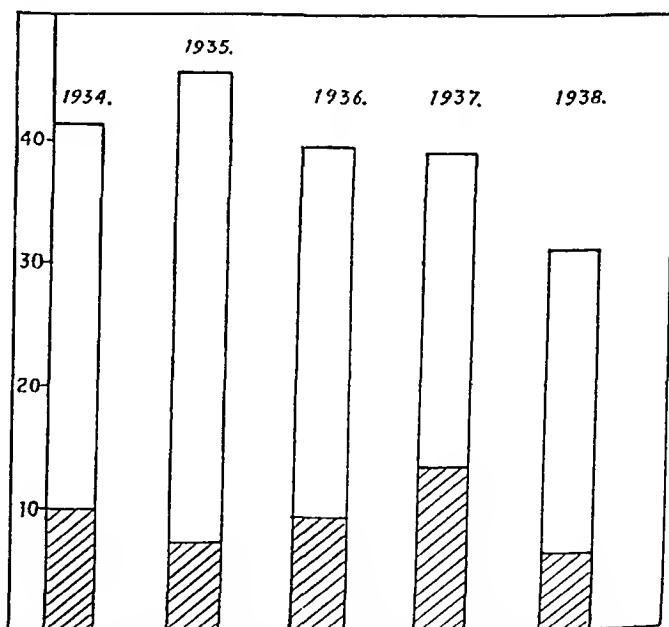


Fig. 3.—Showing average daily sick per 1,000 of the labour force from all causes of sickness and from malaria.

causes are shown, as, when the estimate of malaria incidence rests on clinical diagnosis, a variation of the total sick rate corresponding to and greater than the variation in the malaria

rate is corroborative evidence of the accuracy of the diagnosis.

Figure 4 shows the average daily malaria cases in the main line per thousand of the labour force, month by month, in 1934-37, in comparison with 1938. These figures may be conveniently

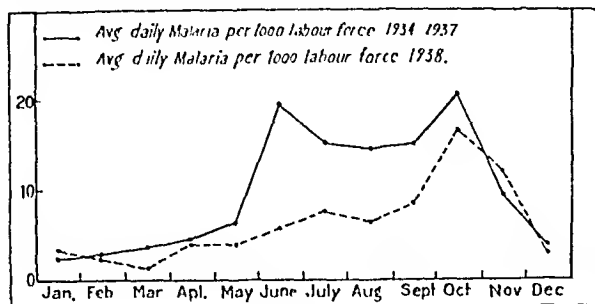


Fig. 4.

summarized, showing the average daily malaria per thousand during the period of treatment—June to September, and after treatment—October to December, with the corresponding average figures for the 1934-37.

		AVERAGE DAILY NUMBER PER 1,000 OFF WORK DAILY DUE TO MALARIA	
		June-Sept.	Oct.-Dec.
1934-37	..	16.0	13.9
1938	..	7.1	11.5

It would appear, therefore, that, although the number of vectors feeding on the main line population in 1938 was at least as great in 1938 as in the previous four years, the amount of clinical malaria was considerably lower during the period when drugs were administered.

(b) The second method of estimating the results of the treatment is by comparison of the incidence of clinical malaria, in the main line and the Namtolla populations. The malaria rates in the two labour forces 1934-38 are shown in comparative form in figure 5. From

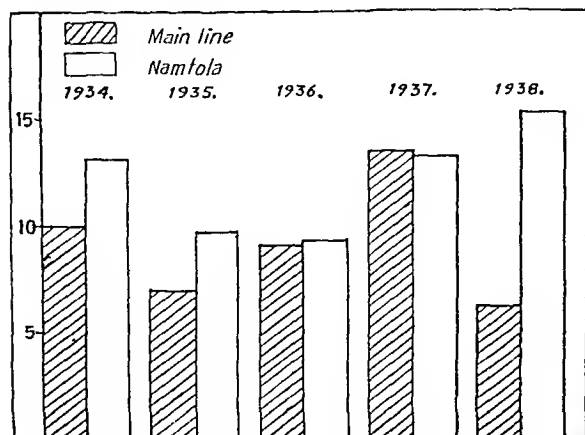


Fig. 5.—Average daily malaria per thousand.

this chart it can be seen that the relationship between the malaria rates in the two populations is not greatly dissimilar in any year in the series except in 1938. The spleen rates in the month of March preceding the drug administration and in March 1939 are as follows :—

	Main line	Namtolla
Spleen rate, March 1938	50 (390 examined).	78 (175 examined).
" " " 1939	38 (406 examined).	83 (109 examined).

From 1934-37 chart 5 shows that an increase in malaria in one population is associated with an increase in the other, the Namtolla population generally showing, as would be anticipated from the 1938 spleen rates, a higher proportion of cases. The rates may be summarized for comparison as follows :—

		AVERAGE DAILY NUMBER PER 1,000 OFF WORK DUE TO MALARIA	
		Namtolla	Main line
1934-37	..	11.25	10
1938	..	15.0	6

In 1938, there was thus a slight increase of malaria in the Namtolla population over the average for the past four years, whereas in the main line population, malaria was reduced by 40 per cent approximately, on the average, for the past four years. This would appear to support the view that the reduction of malaria in 1938 in the main line population was the direct result of the exhibition of drugs.

(c) The results obtained in the three groups A, B and C in the main line population are shown graphically in figures 6 and 7. Chart 6 shows the number of persons attacked with malaria in each group, week by week, from the week ending 22nd May, when the blanket treatment with atebirin was given to group A, until the end of the year. The figures shown in chart 7 may be conveniently summarized as follows :

		NUMBER OF CASES OF CLINICAL MALARIA		
		A	B	C
During 20 weeks' treatment During 13 weeks after discontinuing treatment.		77*	111	151
		127	105	77
TOTAL	..	204	216	228

\* Of these 77 cases 25 occurred in the three weeks between 12th September and 1st October during which period only one treatment was given.

The number of persons attacked with clinical malaria was reduced in both the treated groups as compared with the untreated. So long as treatment was being administered there was

actually a reduction of 49 per cent cases in the atabrin-treated group and a reduction of 26.5 per cent in the quinine-treated group, as compared with the untreated group, and the reduction would certainly have been greater in the atabrin group if two weeks' treatment had not been omitted in the month of September. This fact and the fact that only 84 per cent of the persons in the group on an average received the dose in any one week is sufficient to account for a lower reduction than that of 75 per cent, which was reported by Field in his experiment with the same adult dose.

As soon as the mass treatment of groups A and B was discontinued there was an increase in the number of cases from these two groups, the number of persons attacked being considerably greater than in the control group C. There was an increase of 65 per cent in the atabrin-treated group and an increase of 36 per cent in the quinine-treated group as compared with the untreated group in the 13 weeks following the discontinuance of the mass treatment. The results are shown also graphically in chart 7 which represents the new cases of clinical malaria in each group in the five periods of four weeks, during which treatment was being given and the subsequent three periods of four weeks, when treatment had been discontinued.

#### 10. Conclusions on clinical prophylaxis

In this experiment it was not found possible to undertake extensive blood examinations. The nature of the results, however, so far as clinical cases are concerned, is very similar to those obtained in the Malayan experiment where it was shown that during the period of mass administration the number of clinical cases was reduced in both treated groups, the greater reduction being in the case of the atabrin group, and that subsequent to discontinuing the mass treatment there was an increase of clinical malaria in the treated groups above the control group, the greater increase being in the case of the atabrin group.

In the Malayan experiment it was shown that during the period of treatment, both the gross parasite rate and the gametocyte rate were reduced in the treated groups as compared with the untreated. An analysis of the figures given shows, as has been previously mentioned in this report, that during the period of treatment whereas the untreated group has an average gametocyte rate of 16.6 per cent the gametocyte rate of the quinine and atabrin group, respectively, were reduced to 8.8 per cent and 1.2 per cent. Their figures further show that subsequent to discontinuing the treatment both the gross parasite rate and the gametocyte rate rose in the groups that have been treated, to figures

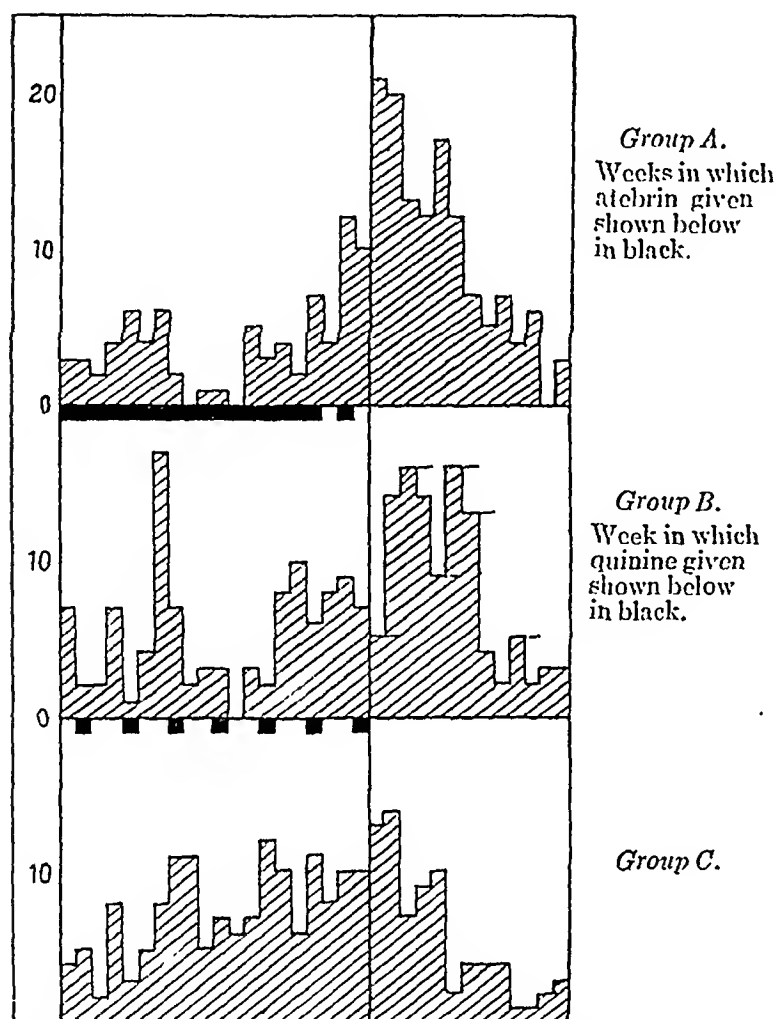


Fig. 6.—Showing new attacks of malaria each week in each group from commencement of treatment.

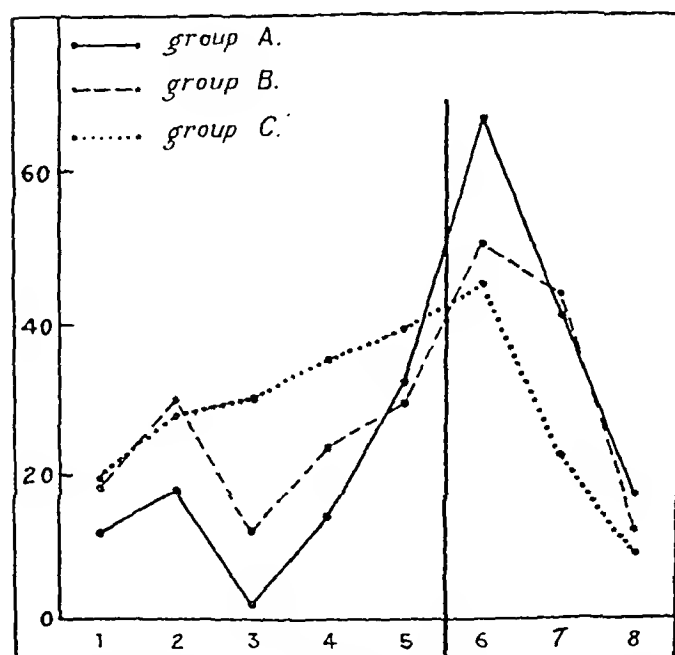


Fig. 7.—Showing new attacks of malaria in the three groups in the five periods of four weeks of treatment and the three periods of four weeks after discontinuing treatment.

considerably greater than those in the untreated group.

It would seem reasonable, in view of the similar findings obtained in clinical cases in the Towkok experiment to those in the Malayan, to assume that similar changes in the gross parasite rate and the gametocyte rate occurred in the population in this experiment.

The question that immediately presents itself from these facts is, why should the incidence of malaria in the treated groups be greater than in the untreated, in the post-treatment period? Field and his co-workers in their paper state 'it is to be concluded that the "sterilization value" both of atebirin and quinine is low when the drugs are given in doses and at intervals appropriate for prophylaxis'. They stated in their conclusion that they believed the 'post prophylaxis' malaria was due to the reappearance of infections which had been clinically, and in many cases parasitologically, 'hidden' by the prophylactic treatment. Do the results from the experiment at Towkok confirm this view? Attacks of clinical malaria in this population between mid-May and the end of the year may have resulted from infections occurring either at some time previous to treatment, or during the period of treatment, or in the post-treatment period. In each group there had been at any time equal risk of infection. Of the cases of clinical malaria which occurred in the unprotected group between mid-May and December, some of these were undoubtedly the result of infection prior to May. Opinion is divided as to what proportion of cases recrudescence in the year following infection, but it is generally accepted that a substantial proportion of cases that receive only a few days' treatment in an attack, as is the case with tea estate labour, will relapse in the following year. Group A, however, had been given a blanket treatment with atebirin in mid-May for 5 consecutive days with a view to sterilizing the blood of this group and actually 83 per cent had received the full treatment and 92 per cent had received 4 or 5 days. This being so, it seems reasonable to suppose that, if a blanket treatment with the dose administered is successful—at any rate in a proportion of cases—in sterilizing the blood, at the end of May a smaller number of persons would have parasites in their blood and be liable to recrudescence in group A than in group C, yet between mid-May and the end of the year there were 204 cases of clinical malaria in group A and 228 in group C. This fact would seem to suggest that the post-treatment increase of malaria in the atebirin group was caused not only by infections that had occurred and been kept latent during treatment becoming manifest when treatment was discontinued, but also that the treatment had actually reduced the natural resistance allowing a higher proportion of infections subsequent to mid-May to become manifest in clinical malaria in group A than in group C. The alternatives to this supposition would appear to be that

either no more than 10 per cent of the cases occurring in group C between mid-May and December were attributable to infection contracted before mid-May, or that the blanket treatment almost completely failed to effect sterilization of group A. Both these alternatives seem rather improbable.

An analysis of the results of this course of treatment would appear to suggest strongly that although the evidence is inconclusive, the benefits effected in reduced incidence of malaria in this population living in an area where biological control presents special difficulties, by the expenditure on clinical prophylaxis in the manner in which it was administered were greater than those effected by expenditure of the same sum on temporary biological control.

The results also make it evident that the malaria incidence at any particular period in the transmission season can be more readily controlled by clinical prophylaxis than by biological methods.

Militating against these advantages is the fact that very much greater difficulties are encountered, due to unpopularity of prophylactic treatment, with an illiterate labour force and much more supervision is necessary to insure success of clinical prophylaxis than in biological control.

In considering the relative merits of atebirin and quinine in the doses in which these drugs were administered, atebirin lowered the incidence of clinical malaria to a greater extent than did quinine, during the period of treatment, and atebirin had the great practical advantage that it caused no unpleasant symptoms, is not unpleasant to take, and needed only one mass treatment weekly. Atebrin in prophylactic doses, as has been shown by other workers, is of much greater gametocidal value than is quinine, and it would appear that this action was responsible mainly for the apparent reduction of clinical malaria in the untreated group in the population.

The expenditure on the atebirin course in this experiment was about seven times as high as the expenditure on quinine, unfortunately the evidence obtained is quite inadequate to make any precise estimate of the relative returns on the expenditure; it may however, be borne in mind that, in the Malayan experiment, carried out with a slightly larger dose of atebirin and a considerably larger dose of quinine, during treatment the average gametocyte rate was in the quinine group nearly seven times as large as in the atebirin group. As the evidence clearly suggests this reduction in the clinical malaria of this population as a whole was mainly ascribable to the reduction in the gametocyte rate, this coupled with the other advantages atebirin possesses over prophylactic quinine certainly justifies a very much higher expenditure on this drug than on quinine for purposes of prophylaxis.

One important character of atebirin demonstrated by Field, that is given additional stress by this experiment, is that discontinuation of the

prophylactic course is liable to be immediately followed by a great increase in clinical malaria, and the evidence from this experiment suggests that possibly this increase is due not only to the infections which are kept latent by the prophylactic course becoming manifest when the attack is discontinued, but that natural immunity may be temporarily impaired.

In view of this it would seem advisable, if atebirin is used prophylactically, that it should be given regularly throughout the transmission season until the close of the season. With regard to the value of a blanket treatment, there is insufficient evidence to draw any conclusion. The cost of the blanket treatment was as great as five full weeks of the subsequent treatment. Field has shown that with the same prophylactic dose, not preceded by a blanket treatment there was a reduction of 75 per cent clinical malaria as compared with his 'control'. This 'control' no doubt was indirectly and advantageously affected by the treatment, so the reduction in clinical malaria brought about by the dose was almost certainly something greater than 75 per cent. In view of these facts I would suggest that a blanket treatment at the conclusion of the prophylactic course would probably be more advantageous than at its commencement, at any rate in instances where only a proportion of a population receive the course.

#### 11. *The economic factor*

The method of control of malaria and the expenditure on control in an industrial population obviously must be governed by certain practical considerations, such as the cost of the disease to the industry in loss of life, working days and efficiency, and on the practicability and economic cost of the various methods of control, such as permanent biological methods, temporary biological methods, or clinical prophylaxis. In this particular population where permanent biological control offered special practical difficulties, and the benefit obtainable by an economic outlay on temporary control appeared doubtful, clinical prophylaxis seemed to be a more economic method of control. The full dose of gramme 0.3 to the entire population weekly recommended by the makers and administered throughout the whole transmission season and terminating with a blanket treatment might obtain a hundred per cent decrease in malaria, and be economically sound in a highly-paid skilled population resident in a hyperendemic area. Such a course, however, at the present cost would almost certainly be an uneconomical method of controlling malaria in any Northern India tea estate labour force, but on the other hand it would appear from this experiment, in which a substantial reduction was brought about by administering a small dose of atebirin to one-third of the population for two-thirds of the transmission season, that atebirin may prove an economic method, in certain cases,

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## THE MODE OF ORIGIN AND PROGRESS OF ANÆMIA IN PREGNANT TEA GARDEN COOLIES\*

By K. P. HARE, M.B., B.S.

Hoogrijan

### *Introduction*

THOUGH extensive studies have been made of the subject, many gaps in our knowledge of the anæmias complicating pregnancy still exist. These gaps are particularly noticeable when information is sought concerning the origin of anæmia, chiefly because most of the workers on the subject have been dealing with uncontrolled populations. I use the word *origin* instead of *onset* advisedly, because it implies some knowledge of the ætiology of the disease and it is probable that more information about the onset will provide the clue to the ætiology of the disease. I have therefore taken advantage of my position as medical officer to a controlled population to study the onset and development of these anæmias. This work has been only the spare time occupation of a general practitioner, so that the amount of material is small and conclusions drawn therefrom await confirmation by other workers in the field. I shall feel satisfied if I can stimulate others who are in daily contact with tea garden labour to record their experience.

### *Material*

This paper is based mainly on a series of 31 women who were found to be anæmic at all stages of pregnancy, and in part on a study of 182 women who were found to be anæmic after the 28th week of pregnancy, 107 of whom it was possible to assign to definite hæmatological groups. The latter series was detected during routine examinations of all women receiving pregnant leave in a group of 13 estates over a period of 12 months in 1938, and has been fully analysed in a paper which appeared in the April number of the *Indian Journal of Medical Research*. The former series was detected in 1939

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\* Read at the Annual General Meeting, Assam Branch B. M. A., Shillong, 1940.

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(Continued from previous column)

of reducing malaria in a low-paid unskilled labour population. Further work could I think with advantage be done to determine the best method of administration in order to obtain the maximum results with the minimum outlay.

### REFERENCES

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Field, J. W., Niven, J. C., and Hodgkin, E. P. (1937). *Bull. Health Organization, League of Nations*, Vol. VI, p. 236.



in the following manner. During January 1939 an accurate list was prepared of every woman of child-bearing age on one estate. During February and March each of these women was seen on two occasions and examined for clinical signs of anæmia. Every case so detected was treated and her name was temporarily removed from the list: any found to be pregnant were struck off the list altogether. It was therefore possible to say that at the beginning of April every woman of child-bearing age was either clinically non-anæmic or was under treatment and would not be restored to the list until completely cured. The few who were both pregnant and anæmic were not considered in this investigation.

These monthly inspections have continued and, in fact, the last one is now in progress but this paper deals only with the story up to the end of January. From April onwards every woman found to be anæmic was further examined as to pregnancy. If not pregnant she was treated and her name was not restored to the list until she was definitely cured. If pregnant she was subjected to a series of monthly hæmatological examinations. This method enabled one to say with some accuracy at what period of the year and at what period of her pregnancy each case became anæmic and also made it possible to observe the progress of each case.

#### *Hæmatological classification*

The classification of anæmias in pregnancy which I have adopted divides these cases into four groups as follows:—

A. A microcytic-hypochromic group in which the mean corpuscular volume is below 85 cubic microns and mean corpuscular hæmoglobin below 22 micro-microgrammes. Stained films of this group show obvious microcytosis and, usually, vacuolation is marked.

B. A normocytic hypo-orthochromic group in which the mean corpuscular volume usually lies between 85 and 105 cubic microns and the mean corpuscular hæmoglobin is under 30 micro-microgrammes. The stained films of this group are remarkable for the uniformity of cell size. There is practically no anisocytosis.

C. A micro-macrocytic hypo-orthochromic group in which the mean corpuscular volume usually lies between 85 and 110 cubic microns but may be higher and the mean corpuscular hæmoglobin is always below 30 micro-microgrammes. The stained films of this group show very marked anisocytosis and nucleated reds are found in the majority of cases.

D. A macrocytic-hyperchromic group in which the mean corpuscular volume is always above 100 and usually above 110 cubic microns and the mean corpuscular hæmoglobin is above 30 micro-microgrammes. The stained films of this group usually show recognizable macrocytosis and always show normoblasts and

megaloblasts\*. In practice some orthochromic cases require inclusion in this group.

The percentage incidence of the various groups in the two series is shown in table I.

TABLE I

*Percentage incidence of hæmatological groups in two series*

Hæmatological group	1938 series	1939 series
Microcytic .. ..	49.5 per cent	48.4 per cent
Normocytic .. ..	14.9 "	12.9 "
Micro-macrocytic ..	23.4 "	29.0 "
Macrocytic .. ..	12.2 "	9.7 "

It is obvious that no significant difference exists between the two series.

#### *Features of the onset of anæmia*

I was able to show that, in the 13 estates in my charge, the incidence of anæmia in the third trimester of pregnancy during 1938 was fairly uniform throughout the year with the exception of the third quarter, July, August and September, when there was a definite increase which was statistically significant. The distribution of cases in the 1939 series in each hæmatological group according to the quarter in which they became anæmic is shown in table II.

TABLE II

*Seasonal distribution of cases according to month of onset*

Quarter	HÆMATOLOGICAL GROUPS				TOTAL
	A	B	C	D	
April, May and June ..	2	2	2	1	7
July, August and September.	7	2	5	1	15
October, November and December.	5	<i>Nil</i>	2	1	8
January, February and March.	1	<i>Nil</i>	<i>Nil</i>	<i>Nil</i>	1

It is obvious that the third quarter of the year is the period of heaviest incidence of anæmia and this appears to apply with greater force in the

\* We raised the question as to whether these cells were true megaloblasts, to which the writer replied:—  
‘These are the marrow megaloblasts with basophil cytoplasm and a dense rosy nucleus. They are not, of course, the “megaloblast of Ehrlich” of pernicious anæmia. There seems to be a very marked division of opinion about the nomenclature of these cells—they seem to me to be more primitive than erythroblasts’.

From the description we do not think that these would be considered to be megaloblasts by most workers; the ordinary megaloblast has a finely-stippled nucleus: the particular cells described seem to us to be more like erythroblasts, or perhaps what some workers describe as ‘macroblasts’.—EDITOR, I. M. G.]

case of group C but the difference is not statistically significant.

Among the cases detected almost every period of pregnancy was represented. The earliest case was 11 weeks' pregnant and two women remained healthy until the 38th week of pregnancy. The distribution of cases according to duration of pregnancy at onset is shown in table III.

TABLE III

*Distribution of cases in 1939 according to duration of pregnancy at onset*

Duration of pregnancy	HÆMATOLOGICAL GROUPS				TOTAL
	A	B	C	D	
10 to 19 weeks ..	3	2	1	1	7
20 to 29 „ ..	8	1	5	1	15
30 to 39 „ ..	4	1	3	1	9
Average duration in weeks.	24.6	23.0	25.0	21.7	24.3

It is evident that, though anæmia may arise at almost any period of pregnancy, it is much the most likely to do so during the third quarter and this is the case whatever the type of anæmia. Moreover there is no significant difference between the mean values of duration at onset for each of the four groups.

It is seldom possible to obtain accurate information as to a coolie's age, but in every case a note was made of the apparent age. Table IV shows the distribution of cases in each group according to quinquennial age groups.

TABLE IV

*Distribution of 1939 cases according to age at onset*

Age group	HÆMATOLOGICAL GROUPS				TOTAL
	A	B	C	D	
15 to 19 years ..	3	3	3	2	11
20 to 24 „ ..	4	Nil	3	1	8
25 to 29 „ ..	3	1	Nil	Nil	4
30 to 34 „ ..	5	Nil	3	Nil	8
Average age at onset in years.	24.6	20.5	23.2	18.0	23.1

There is a tendency for the microcytic type to occur at any age, whereas the other types more commonly occur before the age of twenty-five. This particularly applies to the macrocytic group but the differences are not significant.

Pregnancies involved in the 1939 series varied from the first to the ninth. The distribution is shown in table VI.

TABLE V

*Distribution of cases according to pregnancy involved*

Pregnancies involved	HÆMATOLOGICAL GROUPS				TOTAL
	A	B	C	D	
1st and 2nd ..	6	2	5	3	16
3rd and 4th ..	7	1	2	Nil	10
5th and subsequent ..	2	1	2	Nil	5

The first and second pregnancies are obviously the most dangerous but this is due to the preponderance of early pregnancies in types B, C and D. The risk of microcytic anæmia is evenly distributed throughout the child-bearing period.

*Effects of maternal anæmia on the mother and the fœtus*

Of the 27 women who had delivered before the end of January 1940, three died as a direct or indirect result of their anæmia. One other patient died four weeks after delivery but this death was directly due to an acute fulminating attack of dysentery which she contracted when her blood picture had returned almost to normal. I therefore propose to ignore this death. Otherwise the distribution of cases and mortality, together with the mortality in the 1938 series, is shown in Table VI.

TABLE VI

*Distribution of cases and mortality in series 1939 and mortality in series 1938*

Hæmatological group	Cases	Deaths	Percentage mortality	Percentage mortality in 1938
A	12	Nil	Nil	3.8
B	4	Nil	Nil	Nil
C	8	2	25.0	12.5
D	3	1	33.3	23.1
TOTAL	27	3	11.1	7.5

Though the mortality in the 1939 series was rather higher than in the 1938 series, the relationship between the various groups as regards case mortality was well preserved.

In the former series I was able to show that the risks of prematurity and of still-birth were enormously increased in anæmic deliveries as compared with those non-anæmic, and that premature still-birth was a very common result of anæmia in pregnancy. This observation has been amply confirmed in the 1939 series as is shown in table VII.

TABLE VII

*Fate of the child in the 1939 series of anæmics*

Hæmatological group	Total cases	Cases	Description	Cases
A	12	7	Full-term Living	7
			Still-born	<i>Nil</i>
		5	Premature Still-born	3
B	4		Living	2
		2	Full-term Living	2
			Still-born	<i>Nil</i>
C	8	2	Premature Still-born	<i>Nil</i>
			Living	2
		6	Full-term Living	3
D	3		Still-born	3
		2	Premature Still-born	<i>Nil</i>
		1	Full-term Living	1
			Still-born	<i>Nil</i>
		2	Premature Still-born	2
			Living	<i>Nil</i>

## TOTALS

Cases	Description	Cases	Percentage
27	Full-term living	13	48.1
	Full-term still-born	3	11.1
	Premature still-born	5	18.5
	Premature living	6	22.2

It would appear that the risks enumerated above are relatively increased to some extent in the macrocytic group but are otherwise fairly evenly distributed throughout the groups.

*Features of the progress of the anæmia*

In a previous paper [Hare (1939a)] I described certain cyclical changes occurring in the blood pictures of untreated cases of anæmia in pregnancy and pointed out that, in that particular series, which was a small one, I had failed to find any evidence of a change from one type of anæmia to another in any case. The same experimental attitude was adopted in the 1939 series and treatment was only given when absolutely necessary.

Of the 15 cases listed as microcytic, none had received any anti-anæmic treatment and three were undelivered on 31st January. None of the remaining 12 had ever been or looked likely to be anything but microcytic and hypochromic. One was an early abortion case, two arose late in pregnancy and two, arising at 30 and 31 weeks, refused to undergo monthly examinations. The remaining seven all showed changes in the blood picture of the same order as those described in the previous paper.

Of the four normocytic cases, one received a short course of iron round about the 28th week, but none showed any sign of alteration of type and all showed the cyclical changes.

There were three macrocytic cases. One was hyperchromic, the others orthochromic. All were macrocytic at their first examinations at

22, 12, and 31 weeks and all received a good deal of treatment with liver extracts, but none showed any alteration in type before delivery. After delivery two became microcytic and the other died.

The number of cases listed as micro-macrocytic numbered nine. Seven of them were of that type at their first examinations, but two originated as typical microcytic-hypochromic anæmias. One was first examined at 11 weeks and altered in type at 23 weeks: the other was first examined at 20 weeks and altered in type at 32 weeks. In the first case the alteration in type was accompanied by a sudden collapse, but in the second the alteration was not accompanied by any symptoms. Of the nine cases, one had not delivered by the 31st January, two arose late in pregnancy and one aborted early. Of the remaining five, four had no treatment before delivery but all showed cyclical changes.

I consider that the facts enumerated above justify the claim that these cyclical changes do occur and provide positive evidence in support of Napier's belief that the microcytic type of anæmia may alter in type. A study of the graphical representations of the changes in the blood picture leads one to believe that the alteration in type is actually an exaggeration of the normal changes and may therefore bear the same explanation. In the former paper I put forward a theory that variation of the foetal demand for hæmopoietic substances, in the presence of a stationary maternal intake, produces the normal variations in the blood picture. If the maternal intake of extrinsic factor drops at the same time as the foetal demand increases, the deficiency is likely to become absolute rather than merely relative. In this way an actual alteration of type would occur. If this is the mechanism, why does not the opposite change (from macrocytic or micro-macrocytic into microcytic anæmia) also occur? I think the reason is that the extrinsic factor deficiency is, so to speak, the dominant deficiency, so that reversal can only be brought about by very heavy doses of liver extract or by removal of the foetal demand as occurs after delivery. In the absence of these two necessities no material reduction in cell size occurs but a reduction occurs in the corpuscular hæmoglobin so that an orthochromic anæmia becomes hypochromic.

*Discussion*

It would appear that, at any rate in the district in which I am working, half the cases of anæmia in pregnancy are microcytic and hypochromic, one-tenth are of the very dangerous macrocytic type, another one-tenth are of the type which I term normocytic and which is, by coolie standards, a mild type of macrocytic anæmia and the remaining three-tenths are of the relatively dangerous micro-macrocytic variety.

Anæmia tends to arise most commonly in the third quarter of the year and the probability is

that the seasonal variations apply equally to all the hæmatological groups. Now it has been shown by Napier and his assistants that while the microcytic type *may* show some correlation with the weight of hookworm infection, what he calls the 'liver-marmite group' is much more intimately related with hæmolysis due to chronic malaria. My own previous work has also shown that splenic enlargement is much more frequent in the macrocytic and micro-macrocytic groups and that chronic malaria plays very little part in the ætiology of the microcytic type. It is very tempting to suggest that the seasonal variation in the incidence of group C coincides with the seasonal variation in malaria incidence but the seasonal variation in group A is similar. Maplestone has shown that the incidence of hookworm infection is not steady throughout the year, but is maximal in the spring and the autumn so that the incidence of microcytic anæmia should show two peaks with a trough between them. Again the uniform distribution of macrocytic anæmia throughout the year suggests that acute, as opposed to chronic, malaria does not play an important part in its incidence. It appears to me that whatever part hookworm infection and malaria play in the ætiology of the different types of anæmia, their action is probably uniform throughout the year and we must look for some other factor to account for the seasonal variation.

It is rather striking that, whatever the type of anæmia, the period of pregnancy at which the majority of cases arise is the same. If the primary cause of each type were different this would be surprising: actually it suggests that in all the groups the primary cause is identical. The observations regarding age and parity may be said to be inter-connected since it is obvious that, in the long run, the majority of the earlier pregnancies will be in the younger age groups. Any theory of causation must take into account the slight difference in age incidence in group D as compared with the others.

I would suggest that the primary cause of these anæmias is excessive foetal demand for hæmopoietic substances where the maternal intake is minimal. This theory, I think, adequately explains many of the puzzles presented by these anæmias. According to the level of the maternal intake the deficiency may be relative or absolute. Absolute iron deficiency (with which may be included deficiency of other minerals and of vitamin C) will cause the most severe cases in group A. Absolute deficiency of the extrinsic factor will be responsible for group D. Relative iron deficiency will cause the majority of the group A cases and relative deficiency of extrinsic factor results in the group B cases. A relative deficiency of both iron and the extrinsic factor is responsible for group C. Theoretically chronic malaria is capable of causing a normocytic hæmolytic anæmia and the anæmia caused by chronic blood loss due to

hookworm infection should be of the microcytic-hypochromic type. Therefore the tendency of these two ætiological factors, which I consider to be accessory factors, will be, on the one hand, to reinforce whatever deficiency may be present, and, on the other, so far as malaria is concerned, to introduce the hæmolytic element into the anæmia.

It might be thought that the younger age incidence in group D militates against this theory since one would expect the deficiency to affect all age groups and degrees of parity equally, as it does in the microcytic group. There is, however, a possible explanation for this. It is believed that the extrinsic factor, though probably not vitamin B<sub>1</sub> or B<sub>2</sub>, is closely associated with those substances, being present in foods which include them and absent from those which do not. Now vitamin B<sub>1</sub> is the anti-beri-beri factor and beri-beri is definitely a disease of young adults. In other words, the difference in age incidence actually supports the dietetic theory of causation and is probably due to early adult life making excessive demands for the extrinsic factor.

This theory of causation also accounts for the variation in seasonal incidence. The bulk of the coolies are able to partake freely of green leafy vegetables from November to March and can still obtain some varieties in April and May but from June to October their intake is virtually *nil*. I am informed that a similar variation in their rice-eating habits prevails. From November to April they normally purchase *dhan* from the market and home-pound it themselves: during some of that period they are using the *dhan* they have grown themselves. From May to October they are dependent on milled rice only. Now Macdonald has shown that a significant difference exists between the mean hæmoglobin of families which normally use home-pounded rice and families which use milled rice, the former having the higher value. I suggest that, during the rains when the rise in anæmia incidence occurs the intake of iron, vitamin C and extrinsic factor is at a minimum.

The only point about the tables dealing with mortality and foetal survival is that they emphasize the wastage due to these anæmias and the urgent need of prophylactic measures against them.

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## A SIMPLE AND EFFICIENT REMEDY IN THE TREATMENT OF SCABIES

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SCABIES in this country is so prevalent and often is so resistant to treatment that it constitutes a curse, not only to the individual afflicted by it but to the surgeon whose field is affected by it. A sure, simple and relatively speedy remedy is one to be welcomed. In preparing this note on the treatment of scabies we were surprised to find that in the Madras Presidency the number of cases admitted to hospitals and dispensaries throughout the year 1938 numbered 884,015 for the whole presidency and that next to the fevers it was the commonest disease treated. In addition to being an affliction to the patient and a source of annoyance to the surgeon, it must also be a source of economic loss and inefficiency to the State.

Following a brief reference in the *Lancet* in 1938 to a form of treatment carried out in Hungary, the scheme there outlined was adopted in the dermatology clinic of the Madura Government Hospital. Its use for over a year has given most encouraging results.

The course of treatment carried out in the hospital clinic is as follows :—

1. Paint the whole of the body below the neck with a 40 per cent solution of sodium thiosulphite (hypo).
2. Allow it to dry for about 15 minutes.
3. Paint with a 5 per cent solution of hydrochloric acid (over the hypo).
4. Allow it to dry for about 15 minutes.
5. Repeat the above treatment after an interval of 2 hours.
6. Give fresh linen.

Repeat on the next day.

The patient must not be given a bath before 12 hours after the conclusion of the second day's treatment. An interval of between 3 to 5 days is allowed before commencing a second course of treatment.

The 40 per cent hypo solution and the 5 per cent hydrochloric acid solution are used in all cases *except* children under 7 years of age in whom half the strength of the above solution is used.

The treatment has been rapidly and highly successful in the papular type of scabies. In the pustular type, however, it has been found too irritant for comfort, and the practice here has been to give the ordinary sulphur ointment treatment in such cases until the pustules dry up, when the case is treated on the same lines as a papular case.

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## A SIMPLE METHOD OF TOMOGRAPHY

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TOMOGRAPHY, planography, stratigraphy, and sectional radiography are the names given to the methods of radiography, by which a particular section or plane of the body can be photographed with the elimination of objects in the planes above and below the one selected.

The work of Grossmann (1935) and others led to the commercial production of an apparatus which has been successfully used by

(Continued from previous column)

### Statistics

Types	Number of cases	Results of treatment	Number of cases
Papular	.. 100	Cured	.. 177
Pustular	.. 8	Relieved	.. 25
Mixed	.. 102	Otherwise	.. 8
Total	.. 210		
Maximum and minimum number of courses given.		Occupation of patients treated.	
		Police constables	8
		Dhobi	.. 2
Minimum number of courses	2	Coolies	.. 205
Maximum number of courses	8	Other important complications.	
Total number of courses for all cases	.. 548	Kahn positive cases	.. 11
Average per case	2.5	Albuminuria	.. 29
Cases that were sent from the surgical wards for pre-operative treatment	17	Glycosuria	.. 1
		Other intercurrent diseases	.. 27

It has been found that almost all the cases complain of a mild burning sensation after application of the hypo solution and in cases where there are pustules the irritation is severe. In 12 cases a few fresh eruptions the size of a pin's head appeared after painting. In these cases the treatment was interrupted for a day or so, and the eruptions quickly disappeared.

In addition, all cases of scabies irrespective of type are given an opening dose of mistura alba and cod-liver oil 1 drachm twice daily.

All other complications such as nephritis, syphilis, etc., are treated simultaneously.

One of the most noticeable effects of this form of treatment is that the itching sensation disappears even with the first course of treatment. By the second or third course most of the cases are cured.

Obvious advantages of this scheme of treatment are that it is relatively clean, and except in the worst cases, hospitalization is unnecessary.

McDougall and others for the study of the anatomy of the lungs and the diseases of various organs. The instrument, as put on the market by commercial firms, is prohibitively costly, though its mechanism is quite simple. The principle of its working consists in moving the x-ray tube and the film simultaneously in opposite directions when the exposure is made. Grossmann's tomograph is a convenient and practical instrument in which the tube is carried by the upper end of a pendulum the lower end of which as it swings, moves a film carrier, which is attached to it, in the opposite direction.

### Physics of tomography

Grossmann (1935) and Andrews (1936) have described recently the principles involved in considerable detail.

In the diagram 1, T is taken to represent the position of the tube, O the object, and ab the

Diagram 1.

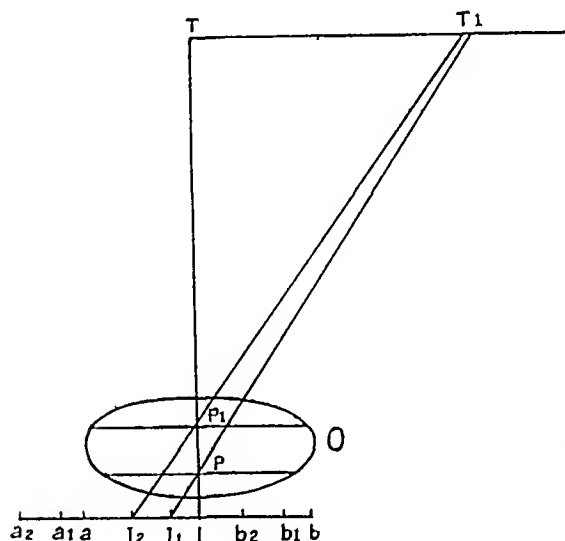
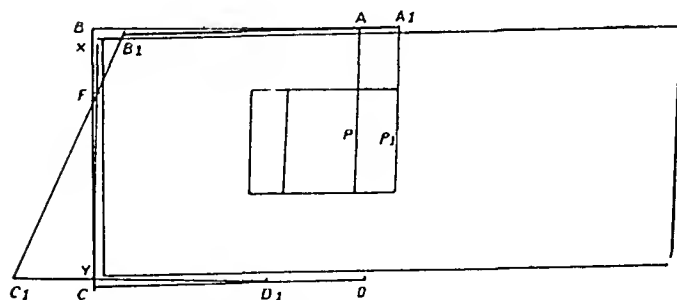


Diagram 2.



film. If P is a point in the plane to be photographed the rays coming from T will cast a shadow of P at I on the film ab. If the tube is moved to the position T<sub>1</sub> the image of P will fall at a point I<sub>1</sub> on the film. If, on the other hand, when T is moved to T<sub>1</sub>, the film ab is moved to a<sub>1</sub>b<sub>1</sub>, the image of P will always fall at the same point on the film. In the same way all the points in the plane of P will cast clear shadows on the film. Whereas a point P<sub>1</sub> in another plane casting a shadow at I on the film

in the beginning will cast a shadow at I<sub>2</sub>, when the tube is moved to T<sub>1</sub>. Hence all the points on that plane will cast only blurred images if the film is shifted from the position ab to a<sub>1</sub>b<sub>1</sub> only. If on the other hand when T is being moved to T<sub>1</sub> the film is moved to a<sub>2</sub>b<sub>2</sub>, so that the point I on the film moves to I<sub>2</sub> the points in the plane through P<sub>1</sub> will cast clear shadows on the film. Hence by varying the extent of movement of the film different planes can be photographed. The principle of any apparatus designed for the purpose consists in fixing the tube and the film to the opposite ends of a rod which is free to have a pendulum movement over a fulcrum which can be fixed at any point along its length. The position of the fulcrum will naturally correspond to the plane to be photographed. By changing its position the different planes in the fixed object can be brought to focus.

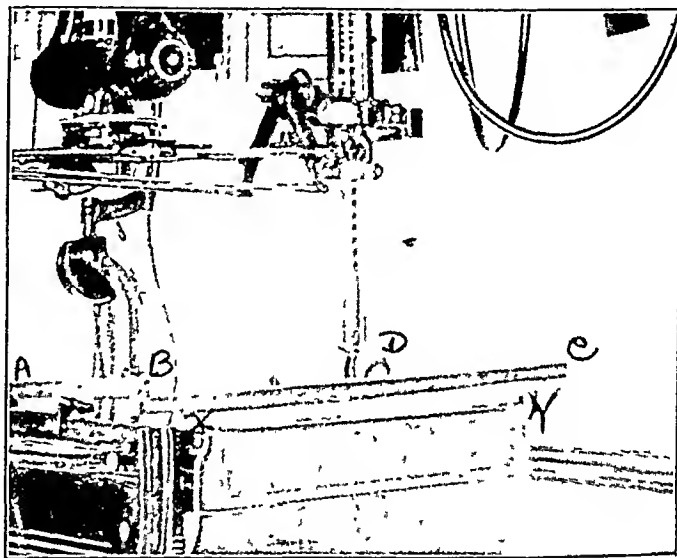


Fig. 1.—Attachment for horizontal tomography.

Another method which has suggested itself to one of us (R. V.), and by which different planes can be focused, is to have fixed fulcrum while the position of the object is changed.

We are of opinion that for tomography a simple cheap contrivance can be designed to be attached to any serviceable x-ray couch, which provides for the free movements of the tube and the film carrier.

The senior writer has designed two attachments, one for taking pictures in the erect posture and the other in the lying-down posture. As suggested by Twining (1937), our attachment is intended to utilize the movable tube stand and the Potter-Bucky diaphragm. The design of the Victor x-ray couch, model 33, is particularly suited for making the attachments easily.

The attachment consists of three wooden pieces AB, BC and CD, hinged at B and C. XY is another piece of wood fixed horizontally to one end of the x-ray table. BC is placed on XY and pivoted to XY at the point F, by means of



a nail which acts as the fulcrum around which BC can be moved in a horizontal plane on XY. A is connected to the film carrier while D is fixed to the vertical stand which carries the tube.

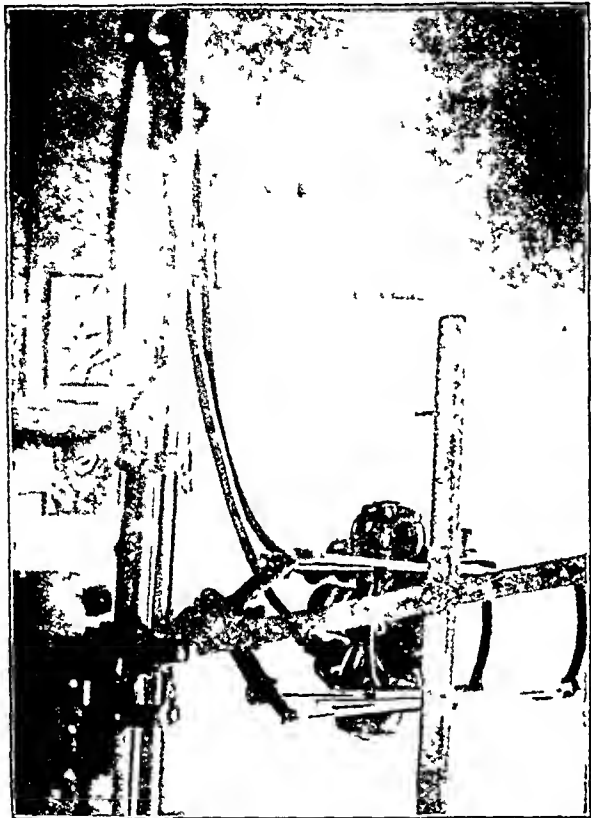


Fig. 2—Vertical attachment



Fig. 3.—Ordinary x-ray picture showing a dense shadow on the left side.

When BC is moved round the fulcrum F, D and A will move in opposite directions. The extent of movement of A and D will depend on the position of the fulcrum F on BC. The point to be remembered in the construction of the attachment is that the length of BC should be equal to the distance between the film carrier and the tube. In that case the distance BF will give the distance of the plane focused from the film. Several holes are made at half-inch intervals on BC, so as to change the position of the fulcrum. For smaller variations of the planes to be photographed, we keep the fulcrum constant while we change the position of the object by interposing cardboards of  $\frac{1}{16}$  inch thickness between the table and the object. By piling up cardboards one above the other the object can gradually be raised and a different plane of the object can be



Fig. 4—Tomograph of the same case showing the presence of cavities in the left upper lobe. The plane focused was two inches behind the sternum.

photographed each time. The tube stand is drawn by a string going over a pulley which is fixed to the C end of the table. The other end of the string is connected to a weight which if let down will automatically pull the tube. The operator holds on to the tube stand by another string which he lets go simultaneously with the making of the exposure. The tube will move in the direction DC, from D to  $D_1$  while the film carrier P connected to A will move in the opposite direction to the position  $P_1$ .

The attachment for taking a tomograph in the erect posture is based on the same principle of utilizing the movable Potter-Bucky and the tube stand, though with necessary modifications

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## STREPTOCOCCUS PYOGENES IN THE THROATS OF A SAMPLE OF HEALTHY INDIVIDUALS

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SWABS taken from the tonsils and naso-pharynx of 300 apparently-healthy individuals were examined for the presence of *Streptococcus pyogenes* and certain other organisms. The individuals examined were from a heterogenous group of healthy persons who for various reasons had occasion to visit the laboratory. As it was not possible to arrange for repeated examinations of a large series of persons the results recorded are based on a single examination of each individual.

Records were maintained of the nationality, residence, occupation, sex, age, general health, history of any past throat infection, state of the gums, teeth and throat of each individual. A throat swab was firmly rubbed over both tonsils

(Continued from previous page)

in its design. In this the film carrier and the tube carrier are connected by a horizontal rod which is pivoted to a fixed vertical rod, so much so that the former is free to move round the pivot in a vertical plane.

We have also found it possible to connect the film carrier and the tube carrier by strings carried over a multiple pulley adjusted in such a way that when the tube moves a certain distance the film carrier will move in the opposite direction over a requisite smaller distance. This method is now under trial.

The results achieved by us are quite comparable to those of others with the use of more costly instruments. The accompanying photographs bear testimony to it. The attachment costs less than two rupees to make.

Tomographic studies are of immense value in thoracic surgery. As it is not adequately recognized in India we hope that the publication of this paper will encourage the wider use of this method of radiographic studies by means of the simple and exceedingly cheap contrivance we have described.

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and the posterior pharyngeal wall and the inoculation of media made soon after taking the swab.

The charged swab was smeared on 8 per cent defibrinated rabbit-blood agar and the plate incubated aerobically at 37°C. The next day any suspicious colonies (fine colonies about the size of a pin's head surrounded by a zone of  $\beta$ -haemolysis) were picked up and inoculated into 10 per cent defibrinated rabbit-blood broth and incubated aerobically. The tubes were shaken occasionally during the first four to six hours of growth—this gave with the haemolytic strains a more uniform haemolysis when the tubes were examined the next day. The growth in blood broth was used for the study of the morphology. Strains were maintained on rabbit-blood-agar slopes. Each strain was plated on heated 5 per cent sheep-blood agar (chocolate blood agar) and the character of any discoloration on this medium noted. The majority of the strains of *Str. pyogenes* produce no change in this medium, but some strains produce a faint narrow zone of discoloration.

The presence of soluble haemolysin was tested for by adding equal quantities of a suspension of 5 per cent washed rabbit-blood cells to an 18 hours' old culture in 20 per cent horse-serum broth, incubating for 2 hours and then keeping in a refrigerator overnight, when the final readings were taken. It is interesting to record that potent haemolysin was obtained by growing a strain of haemolytic streptococcus in ordinary nutrient medium and incubating in an atmosphere containing 10 per cent CO<sub>2</sub> or anaerobically whereas the same strain in the same medium or in serum broth incubated aerobically produced no haemolysin.

Haemolysis was also tested for by the poured-plate method using for this purpose the serum broth culture as the inoculum in rabbit-blood agar. This was most conveniently done by taking a minimal inoculum with a straight fine wire and inoculating into 1 c.cm. of defibrinated rabbit blood placed in a sterile petri-dish, after which 12 c.cm. of melted and cooled nutrient agar was added and the whole mixed by gentle rotatory movement. The haemolysis around the deep colonies was noted after 24 hours' incubation and again after a further 24 hours and 48 hours in the refrigerator. The degree and quality of haemolysis and the character and extension of any haemolytic zones were noted.

The fermentation of lactose, mannitol, sorbitol and salicin (in serum water with Andrade's indicator) was tested with 33 of the 54 strains of haemolytic streptococci isolated.

In a series of 50 examinations primary inoculations were made both on horse-blood agar and on rabbit-blood agar. The number of isolations of *Str. pyogenes* on these two media were approximately the same and as it was more convenient to use rabbit-blood agar, this medium was used for the examination of the whole series.

In a small series of experiments in which primary cultures were made also on sheep-blood agar, the number of isolations on sheep-blood agar was considerably less than the isolations obtained on horse-blood or rabbit-blood agar.

In another series of 70, primary plate cultures were made in duplicate sets of plates, one set incubated aerobically and the other anaerobically (in McIntosh and Fildes' jar). The number and percentage of isolations of *Str. pyogenes* in the two sets of plates are given in table I.

TABLE I

The number and percentage of plates yielding *Str. pyogenes* when incubated aerobically and anaerobically

Incubation	Number and percentage of positive isolations
Aerobic ..	11 or 16 per cent
Anaerobic ..	16 or 23 "

Although the difference of isolation in the two series is not of statistical significance it appears that incubation under anaerobic conditions gives better results. This agrees with the conclusion arrived at by Topley and Wilson (1936) that it is desirable that primary plate cultures should be incubated anaerobically rather than aerobically. A further advantage of the anaerobic incubation of surface-spread plates from primary culture is that the hæmolytic zones are better developed in plates incubated anaerobically and there is distinctly less growth of other organisms than in the plates incubated aerobically. The colour of the medium remains unaltered longer under anaerobic conditions than under aerobic incubation. As however it was not convenient to employ anaerobic method of cultivation for the whole series the results recorded in this paper are based on the findings obtained with aerobic incubation.

The examinations of the other organisms reported in this paper were carried out according to well-known standard methods and need not therefore be given in detail here. The further identification of the alpha hæmolytic streptococci or the viridans streptococci into different species was not attempted but they are grouped together as viridans group.

The results of the examination of swabs taken from the tonsils and nasopharynx of 300 apparently-healthy persons are summarized in table II.

No significant difference was found in the frequency of isolation of *Str. pyogenes* from—

(a) perfectly healthy looking throats (*Str. pyogenes* isolated from 21 or 15 per cent of the 140 examined) and throats showing varying degrees of congestion but without any clinical symptoms (*Str. pyogenes* isolated from 33 or 20 per cent of the 160 examined),

TABLE II

The frequency of *Str. pyogenes* and certain other bacteria in the nasopharynx of 300 apparently-healthy individuals. These results are based on a single examination of each person

Organism	Number of persons from whom isolated	Percentage of persons from whom isolated
<i>Str. pyogenes</i> ..	54	18
<i>Str. viridans</i> group ..	141	47
<i>Str. alpha</i> prime type ..	17	57
<i>Hæmophilus influenzae</i> (hæmolytic type).	156	52

(b) throats heavily stained with 'betel mixture' ('pan') and those not stained or of non 'pan-eaters';

(c) throats with accompanying pyorrhœa and without any pyorrhœa.

It must be noted, however, that the numbers examined in each group are not sufficient to demonstrate any small significant difference in the various groups. The number of persons examined during the cold weather (November to February) and the hot weather (March to June) and the results obtained are shown in table III.

TABLE III

The number of persons examined in the cold weather (November to February) and in the hot weather (March to June) and the number and percentage of isolation of specified bacteria

	COLD WEATHER. NUMBER EXAMINED 187		HOT WEATHER. NUMBER EXAMINED 113	
	Isolated from	Percentage	Isolated from	Percentage
<i>Str. pyogenes</i> ..	29	16	25	22
<i>Str. viridans</i> group	82	44	59	52
<i>Str. alpha</i> prime type	6	3	14	12
<i>Hæmophilus influenzae</i> (hæmolytic type).	100	53	54	48

Thirty-three of the 54 strains of the beta-hæmolytic streptococci isolated from the throats were examined by the precipitin test with type serum of group A, other sera were not available. The method of the preparation of the precipitating serum and the method of testing were according to the methods advocated by Lancefield (1933). Twenty-three or 67 per cent of

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## NATURAL LEPTOSPIRAL INFECTION IN THE RAT POPULATION OF CALCUTTA

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Soon after the discovery of the causal organism of Weil's disease by Inada and Ido (1915), the proof was forthcoming that rats which harbour the organism in their kidneys are responsible for the dissemination of the disease. The presence of natural leptospiral infection in wild rats was first recognized by Miyajima in Japan [Walch-Sorgdrager (1939)]. Since then it has been found to exist in many parts of the world, even in areas where leptospiral infection in man is unknown. For example, in New York the incidence of natural infection in rats is enormously high (about 60 per cent), but no case of the disease among human beings has so far been recorded. In Calcutta Knowles (1928) examined 180 rats, but none were found infected. Later on, the same observer (Knowles, 1932) discovered two infected rats out of 193 examined. But unfortunately the leptospira could not be isolated and identified. After the isolation of *L. icterohaemorrhagiae* from a human case of acute haemorrhagic jaundice (Das Gupta and Chopra, 1937), the present writer undertook a

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the 33 strains of haemolytic streptococci so examined fell into Lancefield's group A.

The strain of *Str. pyogenes* isolated from the throat produced acid but no gas in salicin, lactose, and no change in sorbitol or mannitol. The fermentation of the sugars was as a rule slow and the final reading was taken after 14 days' incubation. Twelve strains of *Str. pyogenes* were tested for pathogenicity by intraperitoneal inoculation into mice and were found to kill the animals in 1 or 2 days.

### Summary

Swabs taken from the tonsils and nasopharynx of 300 apparently-healthy individuals showed the presence of haemolytic streptococcus in 54 or 18 per cent of the persons examined. Of the 54 persons from whom haemolytic streptococci were isolated 33 or 67 per cent yielded streptococci belonging to Lancefield group A, or that approximately 10 per cent of the sample of population examined were carrying *Str. pyogenes* (Lancefield group A). These observations stress the fact that haemolytic streptococci occur not only in pathologically affected tonsils but also in the throats of normal persons.

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systematic examination of rats with a view to demonstrating the infection and identifying the spirochaete with reference to its serological classification. Three hundred and ten rats were examined; out of this number 230 animals were trapped in or near the patients' houses.

### METHODS EMPLOYED

#### I. Microscopic examination of the kidney substance

It has been the experience of several workers that in rats leptospiræ are found exclusively in the convoluted tubules of the renal cortex, and even then only here and there. Large portions from the cortex of both kidneys were, therefore, ground up with sterile sand in an agate mortar and emulsified in physiological saline. The emulsion was examined under the dark-ground illumination.

#### II. Inoculation of susceptible animals

Kidney emulsion was prepared as above and filtered through coarse muslin before inoculation. As a sufficient number of young guinea-pigs were not available, material from six rats was pooled and 2 cubic centimetres of the mixture were injected intraperitoneally into one guinea-pig, except in the cases in which leptospiræ could be demonstrated in their kidneys by direct microscopic examination. Leptospiræ were detected only in 5 specimens, and the kidney substance from each of these animals was inoculated into one separate guinea-pig. Of these 5 guinea-pigs, which received intraperitoneal inoculations, 4 did not show any evidence of leptospiral infection during the observation period of two months. The fifth guinea-pig, however, looked very ill on the fourth day after inoculation, and its peritoneal fluid showed a large number of motile bacteria and a few leptospiræ. Lest the animal should die at night and the strain of leptospira be lost, it was chloroformed and its liver, kidneys, and blood were inoculated into 3 guinea-pigs respectively. The animals inoculated with the blood and liver suspension died on the third day. The smears from liver and kidneys were examined, a few hours after death and they showed only bacteria and no leptospiræ. The guinea-pig inoculated with the kidney emulsion survived till the sixth day, when it was moribund. At this stage it was killed and cultures of heart blood, kidneys, liver and spleen were taken in nutrient agar. Pure growth of a motile bacillus of the *Salmonella* group was obtained from the blood and organs. The liver, which also showed a mixture of bacteria and leptospiræ (the former predominating) by direct microscopic examination, was emulsified and a portion of the emulsion was inoculated subcutaneously into one guinea-pig and intraperitoneally into the other. Both these animals showed the mixed infection, as in the preceding series. In order to isolate the leptospira in a

pure state, two pups were inoculated intraperitoneally with the infected liver (showing both leptospira and bacteria), as it was thought that pups which are susceptible to leptospiral infection might prove refractory to infection with the bacteria. One pup (the younger of the two) died of the bacterial infection within 72 hours of the inoculation. Its heart blood gave a pure culture of the same bacillus as was isolated from the guinea-pig. The other pup was chloroformed when its peritoneal fluid showed a few leptospira on the sixth day after inoculation. The entire liver was cut into pieces and ground up in normal saline. A drop of the suspension was examined under the dark-ground illumination, and it showed both the bacteria and leptospira. The whole bulk of the suspension was lightly centrifuged and the supernatant fluid was filtered through the L<sub>2</sub> Chamberland candle. Four guinea-pigs were inoculated each with 3 cubic centimetres of the filtrate. One cubic centimetre was transferred to each of 4 tubes of Vervoot's medium (one tube containing 10 cubic centimetres). In order to ascertain whether the candle was capable of retaining the bacteria, one cubic centimetre of the filtrate was inoculated into nutrient broth and it remained sterile for more than 3 days. One of the 4 cultures in Vervoot's medium showed a pure growth of leptospira two weeks' after incubation at room temperature (22°C. to 28°C.). The concomitant bacillus was thus eliminated. All the 4 guinea-pigs which received inoculations of the filtrate succumbed to leptospiral infection in periods ranging from 13 to 19 days. Cultures of heart blood from one of these guinea-pigs, taken immediately after death, also gave a pure growth of leptospira. The rat leptospira thus isolated, is agglutinated in a high dilution (1 : 10,000) by the serum obtained during convalescence from the patient in whose house this particular rat was caught. The leptospira isolated from this patient had been already found to be homologous with the classical *L. icterohæmorrhagiae* strain.

### III. Serological tests with the rats' serum

The sera of 100 rats including two of the 5 animals which showed leptospira in their kidneys were tested for agglutinating and lytic effects on a human strain of leptospira isolated locally. As soon as the rat was killed, the thorax was opened and blood withdrawn by puncturing the heart with a capillary pipette, as rats' blood has a tendency to clot rather rapidly after their death. Rich living cultures grown in Vervoot's medium, free from naturally developing clumps, were usually used. In a few cases, however, formalized cultures intended for human vaccination were used when suitable live cultures were not available. Four dilutions of the serum, 1 : 10, 1 : 20, 1 : 40 and 1 : 80 were first made. These were then mixed with equal volumes of the culture. In only one instance further dilutions up to 1 : 1,280 had to be made. In many

cases control preparations, using normal rabbits' serum, were also put up. The tubes containing the different dilutions were incubated at 37°C. for 3 hours. At the end of this period these preparations were examined under the dark-ground microscope beginning with the highest dilution.

### IV. Culture of the renal cortex

Small pieces of the tissue were inoculated into Vervoot's medium and incubated at room temperature (22°C. to 28°C.). The cultures were examined under the dark-ground microscope from the 7th day onwards.

### Results of observations on the different methods

1. Leptospira was detected in only 5 specimens. All these animals were trapped in patients' houses, two in one house and the rest in three different houses. The infected rats were identified as follows :—

Three specimens were *Mus decumanus* Pallas, 1 *Bandicota elliotana* Anderson and 1 *Rattus rattus rufescens* (Gray). Eleven specimens showed an infection with *Trypanosoma lewisi*, 8 with *Spirillum minus* and several showed motile bacteria.

2. Fifty-six guinea-pigs were inoculated with the kidney emulsions, 38 remained alive and well during the observation period of 6 weeks. One animal showed a mixed infection with leptospira and a motile bacillus. The remaining ones died of causes other than leptospiral infection.

3. One hundred samples of sera were examined. Only 4 gave positive reaction. Two specimens reacted in a dilution of 1 : 40, and one in 1 : 80. The fourth specimen gave a titre of 1 : 640. Of these 4 positives, 2 specimens were obtained from the animals which showed leptospira in their kidneys. As 3 of these sera yielded only low titres, it was thought that these might be co-agglutinations. So one such specimen (showing an agglutinating titre of 1 : 80 against a local human strain) was also put up against Hond Utrecht (*canicola*), Andamans CH31, Andamans CH11, Rachmat, Swart V. Tienen, Sejro M. 84 and Kantorowicz (classical strain). The results were negative for all these strains except the last-named one which was agglutinated in a dilution of 1 : 100. It is, therefore, quite possible that the rat was infected with the classical *L. icterohæmorrhagiae* strain.

4. Renal substance of 100 specimens of rats were cultured. Thirty-eight specimens, including the 5 in which leptospira were detected by the direct microscopic examination, showed heavy bacterial growth. Only in 6 cases were these bacteria investigated and found uniformly to belong to the Salmonella group. It may be mentioned here that Lal (1939) noted that 14 per cent of Calcutta rats showed an infection with organisms which agglutinated with the sera of both *Bact. ærtrycke* and *Bact. enteritidis*.



The other cultures remained sterile for more than a month.

### Summary

The kidney substance of 310 wild rats trapped in different parts of the city of Calcutta, especially in the infected areas, were examined by the dark-ground illumination and by animal inoculations. One hundred of these specimens were also cultured on Vervoot's medium. Besides, 100 samples of sera from these animals were tested for agglutinating and lytic effects on a strain of leptospira isolated locally from a human case. Leptospiræ were detected in the kidneys of 5 animals. Two other animals gave serological evidence of leptospiral infection. A strain of rat leptospira was isolated by animal inoculation and identified. It was found to be homologous with the classical *L. icterohæmorrhagiæ* strain which is responsible for infection in man in most cases in Calcutta. The animals which showed leptospiræ in their kidneys were identified as *Mus decumanus* Pallas—3 specimens, *Rattus rattus rufescens* (Gray) and *Bandicota elliotana* Anderson—one each.

My thanks are due to the bacteriology department of the school for assistance in the matter of isolation of leptospira from a mixed bacterial infection, and to Dr. Baini Prosad, D.Sc., Director, Zoological Survey of India, for identifying the infected rats. I am also greatly indebted to Prof. Schüffner of Amsterdam for testing a specimen of rats' serum against different serological groups of leptospira.

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## A Mirror of Hospital Practice

### A DERMOID CYST IN THE RIGHT AXILLA

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**History.**—S. K. D., aged 10 years, was admitted to hospital on 7th August, 1939, with a cystic swelling in the right axilla bulging the pectoralis major muscle on that side. His father says that the swelling started painlessly 6 years ago. Lately it became painful and acquired definite tenderness.

**Family history.**—Nothing particular.

**General survey.**—A well nourished, intelligent child with no abnormality, pulse 80 per minute. Respiration 20 per minute. Temperature 97.6°F. Body weight 4 stone 6 pounds.

**Inspection.**—Extent of the swelling—superiorly from beneath the outer half of the right clavicle to the 4th right intercostal space in the mid-axillary line below, medially to just short of mid-clavicular line, posteriorly and laterally to the posterior wall of the axilla, prominent anteriorly and inferiorly in the form of a uniform regular bulge about the size of an orange. It is slightly constricted in its upper part. There are a few prominent veins on the skin over the swelling.

**Palpation.**—(i) No local rise of temperature, (ii) slightly tender, (iii) lobulated, (iv) consistency, cystic, and (v) transillumination test, negative. It lies deep to the pectoralis major.

Examination of blood and urine revealed no abnormality.

**Operation.**—The boy was operated upon on 23rd August, under paraldehyde and ether anaesthesia.

An incision about 3½ inches in length parallel to and just behind the anterior axillary fold was made. After all bleeding vessels were ligatured the swelling was explored at its most dependent part, i.e., in the floor of the axilla. It was found to be cystic and bluish in colour. Lipoma was immediately negatived and a cyst was evident. Dissection was not uneventful although not difficult except near its apex. During manipulation it burst. The fluid which drained out was slimy, shiny, yellowish-green and slightly opaque. The apex was firmly adherent to the adjacent structures and the cyst had to be divided at this part. The remainder of the wall at the apex was dissected out and scissors were used to separate it from a definite fibrous band which extended towards the neck. A drain was put in and the wound was closed with 70° of abduction and 20° of flexion of the arm.

**Post-operative course.**—Uneventful.

**Macroscopic characters of the cyst wall.**—Encapsulated, bilocular with a smaller bulge at the apex. The inner lining was shiny and the thickness was not uniform all through and moderately hard at places.

**Histological characters of the cyst wall.**—(1) Definite fibro-clastic capsule, thick in places and containing inflammatory cells on the outside (Van Geisson's stain—figure 1).

(2) Internal to this was a layer of connective tissue intermixed with elastic fibres and containing the following structures:—

(a) Islands of cartilage, both hyaline and yellow elastic variety (elastic tissue stain—figure 2).

(b) Definite lymph nodes of various sizes (hæmatoxylin and eosin stain—figure 3).

(c) Bundles of unstripped and striped muscle fibres (figure 4).

(d) Islands containing acicular and rhomboid lipoid crystals, with no degenerative change nearby and with



PLATE V



Fig. 1 (low power) showing outer fibro-elastic capsule with blood vessels, round cell infiltration. Inner connective tissue layer showing round cell infiltration.



Fig. 2 (high power) showing cartilage cells and yellow elastic fibres.

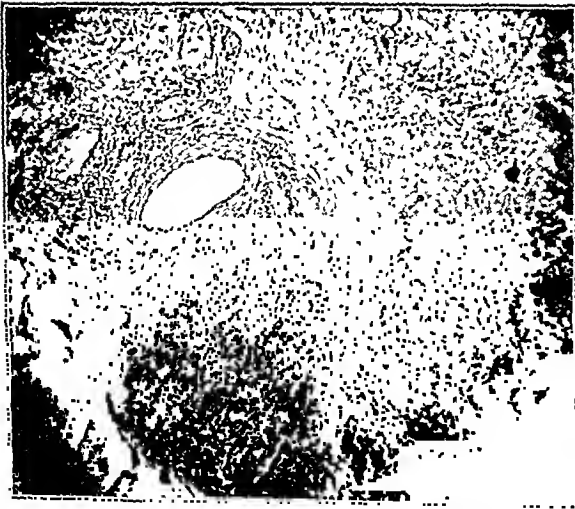


Fig. 3 (high power) showing lymph follicle and blood vessels in the wall and two bundles of muscle.

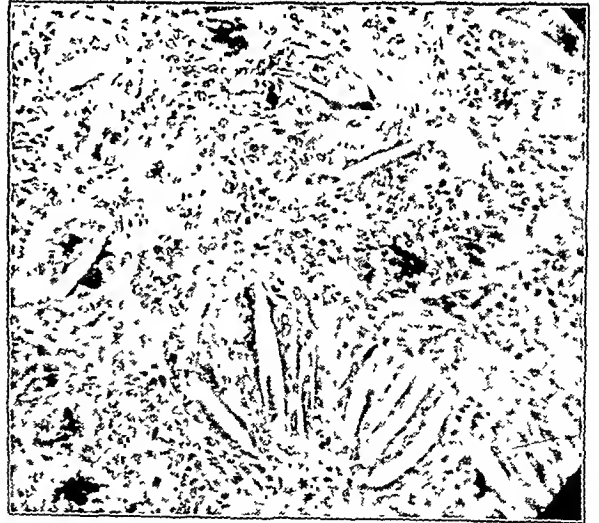


Fig. 4 (high power) showing giant-cells some of which show engulfing lipoid masses and round cell infiltration.



foreign body giant-cells systems round them, many of which are seen with a lipoid crystal in their body (figure 4).

(c) Inflammatory cells.

(3) No epithelium was detectable internal to this.

### Discussion and diagnosis

All these findings show that the cyst is a developmental one and differential diagnosis lies between—

(1) Lymphatic cyst.

(2) Cystic hygroma.

(3) Dermoid cyst (Bidermal) variety of Ewing.

Diagnosis of dermoid cyst is obvious as the other two are ruled out by—

(a) Characters of the contents.

(b) Absence of endothelium lining the wall.

(c) Presence of characters of dermoid of Ewing in its wall.

(d) No penetration in different planes in the axilla and easy enucleation of the cyst.

An attempt is made to explain the possibility of dermoid cyst in the axilla as follows :—In the third week of embryonic development the region of the future neck is occupied by 5 arches separated externally by pharyngeal grooves and internally by pouches. The 4 arches caudal to the first do not meet in the middle line with the fellow on the opposite side externally, but their ventral ends are directly against the pericardial cavity separated by a plane of loose tissue—the sliding plane of Frazer. As the head rises from the primitive dorsal curve of the vertebral axis at the flexure line of the future neck, i.e., just caudal to the second arch (second groove), the region of the neck comes into existence and is an anatomical region when the developing lungs on the two sides in the pericardio-peritoneal channels push the heart caudally. The precervical sinus in the meantime has made its appearance and is bounded cranially by the flexure line of the neck, caudo-ventrally by the epipericardial ridge and dorso-caudally by the elevation caused by the cervical myotomes. On its floor lie the third, fourth and fifth arches with the corresponding grooves. With the development of the neck the precervical sinus is obliterated by the migration of cervical myotomes sub-ectodermally which develop into the future infrahyoid, sterno-cleido-mastoid, trapezius and scalenus anticus muscles. The fourth arch artery of the right side, destined to form the first and second parts of the right subclavian artery, lies in the floor of the precervical sinus in the fourth arch tissues. The fourth arch elements, destined to form the thyroid ala and the constrictors of the pharynx and cricothyroideus, is gradually covered up by migrating cervical muscles and thus these with the right subclavian artery lie beneath the infrahyoid group of muscles, scalenus anterior (covering only the artery) and sterno-cleido-mastoideus. Accidentally, if the attachment of

the floor of the sinus with the fourth arch artery is firm, the muscle migration of the neck may sequestrate a portion of the wall of the sinus field (lined by epithelium) with the developing subclavian artery. This sequestration of a portion of the epithelium-lined wall may contain all the elements of the fourth arch tissue (cartilage, muscle, lymphoid tissue and nerves). Further descent of the fourth arch artery to the adult site caused by the development of the thorax below and the neck above causes a further descent of this remnant. Later when it develops into a cyst, its wall may have one or all of the following characters :—

(a) Epithelial lining, stratified squamous variety, columnar or stratified columnar variety.

(b) Arch tissue derivatives in the wall, muscle, cartilage, lymphoid tissue, etc.

(c) Lipoid crystals in its wall due to absorption from within the cavity, and it may have giant-cell systems (Ewing).

(d) Definite encapsulation.

(e) It develops in the axilla due to the descent of the subclavian artery and barriers in front of it.

(f) It is adherent to the subclavian artery through the apex of the axilla.

With the exception of the epithelium every point above-mentioned is in favour of the cyst. Hamilton Bailey in his study of dermoids especially in the neck (branchial cysts) mentions that the wall of the cyst may be devoid of epithelial lining and suggests that repeated inflammation may account for such anaplastic change. Metaplasia of the epithelium may also occur and thus the various types of epithelium above mentioned are explained. It may be added here that a branchial cyst is a variety of epidermoid (monodermal dermoid of Ewing).

As a corollary to this it may be said that as the fourth arch artery on the left develops into the aortic arch no such dermoids occur in the left axilla in connection with the left subclavian artery. And if and when such a dermoid develops from the remnant of the precervical sinus on the left side it should be in the mediastinum, fixed to the aortic arch by a band of tissue and thus the occurrence of many of such dermoids, if not all, in the mediastinum can be explained. One hundred and ninety-one such cases have been recorded in the literature. Our case is one of bidermal dermoid where the epithelium has suffered the anaplastic change mentioned above and has migrated into the right axilla as a sequestered portion of the precervical sinus.

### Summary

1. Dermoids in the axilla may occur and are of the nature of sequestration dermoids from the precervical sinus of Frazer. It may be an epidermoid (branchial cyst) or a bidermal dermoid.

2. They should occur only on the right side.

3. Many if not all of the sequestration dermoids in the mediastinum are remnants of the precervical sinus and migrate into the thorax with the left fourth arch artery, which develops into the adult aortic arch.

We are indebted to Mr. L. M. Banerjee, Professor of Surgery, Carmichael Medical College, Calcutta, for giving us valuable suggestions and permission to report this case.

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### M. & B. 693 IN PNEUMOCOCCAL INFECTION: TWO CASES\*

By S. C. SEN, L.M.F., D.T.M. (Cal.)

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#### Introduction

CHAND, Taylor and Chitkara (1939) and Taylor and Chitkara (1939) published two interesting reports on pneumococcal meningitis and empyema treated with M. & B. 693.

The efficacy of this comparatively new chemotherapeutic agent has already been proved, and to-day it has established the foremost position among the remedies against certain diseases.

In November last I treated a case of pneumococcal empyema by the method recommended by Taylor *et al.*, that is, by combined aspiration and M. & B. 693, resulting with a success.

*Case 1.*—A male, aged 55 years, was treated for right lobar pneumonia with M. & B. 693 as usual, in the hospital. The temperature came down to 98°F. on the 3rd day of '693' administration, on the 5th day of the ailment. A secondary rise of temperature occurred the same evening and it was subnormal (96°F.) next morning. Since then the patient was apparently doing well except for pain in a localized area over the right side of the chest which persisted from the beginning of his illness.

He had a further rise of temperature on the 8th day after crisis. This assumed the character of morning remission and evening rise.

#### Laboratory findings—

Blood for malarial parasites—negative (thin and thick film).

\* Read at a clinical meeting of the O'Conner Memorial Medical Association, Panitola, Assam.

Sputum—negative for acid-fast bacilli.

Leucocyte count—marked leucocytosis (12,000).

Stools—ascaris eggs ++; hookworm eggs ++; trichuris eggs +.

The diagnosis of post-pneumonic empyema was arrived at, after watching for a few days and having completed the laboratory findings together with careful clinical examination of the patient.

*Treatment.*—He was given M. & B. 693, two tablets morning and evening (2 gm. in a day) for four days only, and an injection of 10 c.cm. soluseptasine. The empyema was aspirated with a 20-c.cm. record syringe and a large-bore needle on the 11th day of the second attack and 19 days after crisis. But only about 2 c.cm. of thick creamy pus could be withdrawn, in which pneumococci were encountered microscopically. On the day of operation the temperature went up to 99°F. in the evening which was lower than in the pre-operative period. From the next day the patient had a normal temperature and said he was feeling much better, the pain, discomfort and night cough being much relieved. He made an uninterrupted speedy recovery without any further aspiration. He was given a mixture containing creosote, potassium iodide, calcium gluconate, aromatic spirit of ammonia and oxymel scillae for a few days during and after the '693' treatment.

The points of interest are:—

The pus was thick and creamy, and only a very small quantity could be withdrawn; but aspiration gave immediate relief to the patient.

The M. & B. 693, however, gave a satisfactory result in smaller doses though it was contrary to the recommendation of Taylor *et al.* that this mode of treatment is not suitable when the pus is thick.

*Case 2.*—A female, 27 years old, was admitted on 27th November, 1939, with severe broncho-pneumonia. She developed acute meningitis on the 3rd day of the disease when she was receiving the usual M. & B. 693 treatment.

Lumbar puncture—the cerebro-spinal fluid was under tension and Gram-positive capsulated diplococci were found microscopically in the films made from it. The serological type of the pneumococci could, however, not be determined. Delirium, restlessness, stiffness of the neck, etc., became progressively worse though eight tablets (4 gm.) were given daily, and four injections of 10 c.cm. each of soluseptasine (M. & B. 137) were also given when oral administration was not possible. The woman eventually died on the 8th day.

It appears that the 693 could not exert its desired influence on the meningeal infection, as the case developed meningeal symptoms during the course of treatment and when the concentration of the drug in the cerebro-spinal fluid was likely to be the same as that of the blood.

Taylor and Chitkara (1939) and Chopra *et al.* (1939) have also reported that sulphonamide derivatives are of little value in meningitis of pneumococcal origin though encouraging results were obtained in meningococcal infection.

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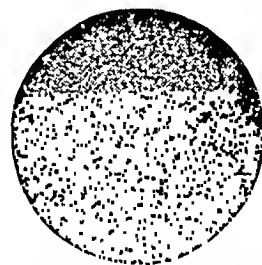
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# Indian Medical Gazette

MAY

## THE STERILITY OF THE SYRINGE

If you suggest to the practitioner and the hospital nurse that his or her method of sterilizing syringes and needles is inadequate and that probably on every occasion that they give an injection they introduce living bacteria, they either express great indignation that you should accuse them of what in their opinion amounts to little short of malpraxis, or the superior tolerance of one who knows better and proceed to describe in detail the methods that they have employed with uniform success for many years.

They firmly believe that the methods they employ are above reproach, or, they would not, we hope, use them, and when occasionally an intramuscular quinine injection suppurates, they blame the patient for contaminating the puncture, or imagine rather vaguely that the tissue-destroying action of the drug formed a necrotic focus into which pyogenic organism circulating in the blood had found their way. Yet, nine times out of ten the methods they employ are grossly inadequate, and probably in ninety-nine times out of a hundred they are short of the ideal and they are only saved from disaster by the fact that the tissues of the body have remarkable bactericidal powers, even when they are damaged by such drugs as quinine or emetine.

It is extraordinary how much faith is placed in alcohol as a disinfectant, when in fact in most circumstances it is not only a very poor one, but may be an actual medium for the spread of pathogenic organisms, as was recently shown by a Swiss worker who collected 13 samples of alcohol from different university clinics in Berne and grew bacteria from 12 of them, in one instance isolating *Clostridium welchii*. Even non-sporing organisms are not killed readily by means of strong alcohol, about fifty per cent alcohol in most circumstances being much more efficacious, but in the presence of serum or pus strong alcohol in particular produces a relatively impenetrable coating of coagulated protein, inside which the most delicate organism may remain alive for a considerable time.

An interesting result of an editorial discussion of the subject in the *British Medical Journal* has been the number of correspondents it has brought out into the open, who have then proceeded to display the inadequacy of the methods on which they rely, sometimes claiming to have 'invented' them, or to offer ridiculous suggestions, such as that syringes should be sterilized by ultra-violet radiation.

It is easier to be critically destructive than constructive and, whilst in a modern hospital

there is no possible excuse for anything short of the employment of syringes scrupulously sterile in all their parts, there may be circumstances in private practice where a thousand to one chance has to be taken, and it is far better for the practitioner to know and face this fact than to bluff himself that his methods are perfect. The most satisfactory method of sterilizing syringes, other than by efficient autoclaving which will not always be possible, is by a combination of heat and antiseptics, that is, by boiling for 10 to 15 minutes in 0.5 per cent carbolic acid solution and drying the inside of the syringe and needle with ether. This takes time and when a practitioner has many calls to make with a high percentage of injections to be given, such a procedure at each house will be wellnigh impossible, but, if the syringe is never used for anything but the injection of sterile solutions intramuscularly or intradermally, it should be sufficient if the body of the syringe is sterilized effectively at the beginning of the day, kept in 70 per cent spirit, handled only with surgically clean hands, and the needles attached only with flamed forceps. The needles can be kept separately in sterilized test tubes or other suitable containers from which they must be removed with sterilized forceps, and each used only once during the day.

The syringe or needle is not of course the only source of contamination of a sterile inoculum; a fruitful source is the rubber cap of the bottle in which it is contained. A casual wipe over with spirit or iodine is all that this usually gets, though such a procedure is quite inadequate if the cap is at all badly contaminated. However, a swab soaked in 5 per cent carbolic acid or other equally strong antiseptic and left in contact with the cap for the 10 to 15 minutes that is being spent in sterilizing the syringe should be efficient.

Another source is the patient's skin: the methods usually adopted—tincture of iodine application followed by thorough swabbing with spirit, or the reverse procedure—will only sterilize the surface. Fortunately, the organisms likely to be found in the sebaceous glands or hair follicles are non-pathogenic, at any rate to the individual in whom they occur, and the only real danger lies in subclinical foci of infection from which organisms may be carried deeper into the individual inoculated, or they may contaminate the needle so that if this is not properly sterilized before use again the infection will be transferred to another individual.

This brings us back to the fact that, even if the body of the syringe is treated as we have suggested above, a fresh needle which has been effectively autoclaved or boiled in carbolic acid solution since it was last used must be attached for each patient.

We would like to add that the practitioner, however busy he may be, should attempt to exercise a little more discipline in his bag than we are afraid is the usual practice; if possible he should keep sterile and septic bags, or at

least have a rigid division, so that at the end of the day his 'sterile' syringes, rubber-capped vaccine bottles and cotton-wool are not mixed up with pus smears, blood specimens and even faeces tubes, and finally let him not forget that

a hundred successful inoculations are no indication that *his* methods were aseptic, nor are a thousand such any guarantee that on the next occasion he will not inoculate living spores of *Clostridium welchii*.

## Special Articles

### HÆMATOLOGICAL TECHNIQUE

#### PART IV

By L. EVERARD NAPIER, M.R.C.P. (Lond.)

and

C. R. DAS GUPTA, M.B. (Cal.), D.T.M.

Calcutta School of Tropical Medicine

#### (7) Determination of corpuscular volume

*Principle.*—A volume of uncoagulated blood is centrifuged at a high speed in a graduated tube until there is no further packing of the corpuscles. The level of packed red cells and of the serum are read off directly from the tube; from this the proportion of the packed cells to the whole blood is calculated and is expressed as a percentage.

#### *Apparatus required*

1. Graduated cell-volume tubes fitted with rubber corks.
2. Capillary pipettes with rubber teats.
3. High-speed centrifuge machine that will rotate at at least 3,000 revolutions per minute.
4. A balance to ensure that the weight of the tubes and their contents are about equal.
5. Hand lens.

*Cell-volume tubes.*—Various types of tubes are in use; these vary in length, bore, and capacity. Wintrobe uses small tubes, 11 centimetres long with a bore of 2.5 millimetres, which are marked in millimetres and centimetres from 0 to 10. In our laboratory, we use a tube 7.5 centimetres long with a bore of 7 millimetres and graduated from 0 to 110. These tubes were specially made for us, by Messrs. Baird and Tatlock, London, to fit in our high-speed centrifuge machine, but comparatively short graduated tubes of this kind are now easily obtainable from instrument makers.

As the degree of packing of the cells depends to a certain extent on the calibre of the tube, it is desirable that the same set of tubes which were used in working out the normal standards should be used in all subsequent work.

*Method.*—The blood is taken in the usual way into a 5-c.cm. or 3-c.cm. flask containing oxalate (see part I). With a capillary pipette withdraw oxalated blood from the flask after it has been well shaken, fill up the graduated cell-volume tube from the bottom upwards exactly up to the 100 mark, put in a small rubber cork to prevent any evaporation during centrifugation, and place it in the centrifuge bucket.

If possible two specimens should be placed in the centrifuge at the same time. In any case, the centrifuge bucket containing the graduated tube must be balanced against a similar bucket and tube so that their weights are exactly equal, before these two buckets are placed in opposite sides of the centrifuge; this elementary principle must be observed rigidly, both for the sake of the centrifuge and for satisfactory packing. Centrifuge at a high speed—2,500—3,000 revolutions per minute—until there is no further packing of the red cells.

The maximum time required for complete packing of the red cells must be found out by a few preliminary experiments. This will depend to a great extent on the centrifuge machine.

The tubes are first spun for 20 minutes at a high speed, the actual speed being noted; they are taken out and the readings taken; they are again spun for another 5 minutes and the readings again taken. The process is continued until there is no difference between two consecutive readings—the time at which the first of these two readings was taken is the time required for complete packing of the cells, as there was no further packing. The mean time in minutes for 10—20 such experiments is taken as the time required for complete packing of cells with that particular centrifuge machine at that particular speed. However, in all subsequent examinations a little extra time, say 5 minutes, should be allowed over and above the mean time determined.

Generally, the cells are fully packed if the tubes are spun for about 20 minutes in a centrifuge-machine at a speed of 2,500 to 3,000 revolutions per minute, but it is safer to allow 30 minutes.

The tubes are now taken out of the buckets and with a hand lens the marking on the tube corresponding to the level of the packed red cells is noted; also the top level of the serum is checked. If this is at the mark 100, then the red cell reading can be translated directly into a percentage, but if it is more or less than 100 the percentage figure must be calculated making an allowance for this fact.

*Example.*—If the top of the serum is at the 102 level and the red cells at 42, the cell volume is  $\frac{42}{102} \times 100 = 41.17$  per cent.

With leukæmic blood it is almost impossible to read the top level of the red cells accurately and therefore it is difficult to ascertain the correct cell volume.

*Anti-coagulant.*—This has been discussed above (part I), but perhaps we should again mention that, if the isotonic mixture of potassium and ammonium, which we recommended, be used, no shrinkage will occur.

On the other hand, if potassium oxalate alone (0.2 per cent) be used, then a factor,  $\times 1.09$ , must be applied to the cell volume before the corpuscular values are calculated.

*Example.*—The uncorrected cell volume is 44 per cent; the corrected cell volume will be  $44 \times 1.09 = 47.96$ .

### (8) Calculation of corpuscular values

From the red cell count, the hæmoglobin expressed in grammes per cent, and the corpuscular volume, certain absolute values can be calculated.

These values are :—

- (1) the mean corpuscular volume (MCV),
- (2) the mean corpuscular hæmoglobin (MCH), and
- (3) the mean corpuscular hæmoglobin concentration (MCHC).

#### Mean corpuscular volume

This is the mean, or average, volume of a single red cell.

It is expressed in cubic microns (cu. $\mu$ ) and is obtained by the following method :—

$$\text{MCV} = \frac{\text{Volume of packed red cells in c.cm. per 1,000 c.cm. of blood}}{\text{Red cells in millions per c.mm.}}$$

*Example.*—Corpuscular volume = 40 c.cm. per 100 c.cm. of blood.  
Red cells count = 5,000,000 per c.mm.  
Mean corpuscular volume =  $\frac{40}{5} = 8.0$  cubic microns (cu. $\mu$ ).

#### Mean corpuscular hæmoglobin

This is the average hæmoglobin content of a single red cell expressed in micro-microgrammes ( $\gamma\gamma$ ).

It is obtained by the following method :—

$$\text{MCH} = \frac{\text{Hæmoglobin in grammes per 1,000 c.cm. of blood}}{\text{Red cells in millions per c.mm.}}$$

*Example.*—Hæmoglobin = 14 grammes per 100 c.cm. of blood.  
Red cells = 5,000,000 per c.mm.  
Mean corpuscular hæmoglobin =  $\frac{14}{5} = 2.8$   $\gamma\gamma$ .

#### Mean corpuscular hæmoglobin concentration

This is the mean, or average, of the hæmoglobin concentration in each cell, and is expressed as a percentage of the cell contents :—

$$\text{MCHC} = \frac{\text{Hæmoglobin in grammes per 100 c.cm. of blood}}{\text{Volume of packed cells in c.cm. per 100 c.cm. of blood}} \times 100$$

*Example.*—Hæmoglobin = 14 grammes per 100 c.cm. of blood.  
Corpuscular volume = 40 c.cm.  
Mean corpuscular hæmoglobin concentration =  $\frac{14}{40} \times 100 = 35.0$  per cent.

That is to say, in this instance 35 per cent of the cell substance consists of hæmoglobin.

The great advantage of these mean values is that, in calculating them, it is not necessary to decide on any arbitrary normal, as one does in calculating indices, e.g., the colour index, for arriving at which one usually considers 5,000,000 red cells per c.mm. and 100 per cent (? of what) to be the normal values. Unqualified, a colour index is a meaningless expression, as even if the above normal values have been taken, it is still uncertain what 100 per cent hæmoglobin means (*vide* part I). If later one decides on the normal values for the particular population, then it is very simple to calculate the colour index.

*Example.*—MCH of the particular case = 35  $\gamma\gamma$ .  
Mean MCH of the population = 30  $\gamma\gamma$ .  
Colour index (CI) =  $\frac{35}{30} = 1.16 = 1.17$ .

Similarly, the volume index and the saturation index can be calculated from the MCV and MCHC, respectively.

There is in our opinion little point in calculating these indices, and we recommend workers to get into the habit of thinking in terms of mean corpuscular values instead of indices, just as they should get into the way of thinking in terms of grammes of hæmoglobin instead of percentages.

*Normal values.*—There are undoubtedly different normal values for different populations. We will consider mean corpuscular volume first: Whitby and Britton give 86 as the mean, with the range from 80 to 94, but neither these writers, nor the majority of others who give a 'normal range', make any attempt to explain what they mean by the 'normal range'. They can scarcely mean that all normal observations fall within the range, but they do not specify what percentage of observations may be expected to fall within it. If one gives the mean (m) and the standard deviation (sd) of a number of observations, that at least does mean something definite, namely that two-thirds of the observations will fall between  $m + sd$  and  $m - sd$ , and that 19 out of 20 will fall between  $m + 2 \times sd$  and  $m - 2 \times sd$ .

The last figures seem reasonable ones for practical purposes and can certainly be applied amongst hæmopoietically more stable populations than we usually encounter in India, but in most of our populations it provides too wide a range. Even for our Calcutta series in which the mean is 90.49 cu. $\mu$ , the range would be  $(90.49 + 2 \times 7.90 =) 106.29$  to  $(90.49 - 2 \times 7.90 =) 74.69$ , or in round figures from 75 to 106 : this is too wide to be considered a normal range, though the mean is close to that given by other workers. On the other hand, some of the Assam, so-called normal, populations have a very low MCV, and if the same rule were applied the range would be ridiculously low, e.g., 57.21 to 85.37 cu. $\mu$  in the first Assam series quoted, but there is evidence in this case that

(Continued at foot of next page)

## THE MEDICAL PROFESSION AND FIRST AID

By KHAN BAHADUR A. HAMID, A.O.St.J., D.P.H.

General Secretary, St. John Ambulance Association (Indian Council), and Organizing Secretary, Indian Red Cross Society

AN important aspect of the social function of medicine is popular health education which should aim at 'levelling humanity up to the

(Continued from previous page)

the whole population is suffering from a degree of iron deficiency anæmia; therefore, as the figures are not based on a truly normal population, this rule cannot be applied.

It is obvious that no hard and fast rule can be laid down. Whenever possible, it is best to examine normal individuals of the population concerned, and, where one can be certain of excluding most of the cases of sub-clinical blood dyscrasia, to calculate the range from the mean *plus* or *minus* twice the standard deviation. Otherwise, 80 to 100 cu.μ may be taken as the normal range for general use in India. That is to say, any figure below 80 cu.μ may be taken as indicating microcytosis and any above 100 cu.μ as indicating macrocytosis.

Similarly, for the mean corpuscular hæmoglobin, on the Calcutta figures the normal range should be  $28.53 \pm 2 \times 2.31 = 23.91$  and 33.14, or roughly 24 to 33γγ. This is in our opinion a good normal range for general use in India; any figure below 24γγ indicates hypochromia and any above 33γγ hyperchromia.

Finally, a good range for the mean corpuscular hæmoglobin concentration is 30 to 35; this is not based on any of the data quoted, for reasons into which we need not go now, but on our general experience.

outlook and attainment of scientific medicine, not levelling it down to the average human comprehension which would be only sovietization of medicine'.

The war has brought to the forefront the importance of the teaching of first aid and home nursing, which is education of the public in giving assistance in time of emergency. First aid is an art based on fundamental principles of practical medicine and surgery. This knowledge is imparted in order to enable trained persons to give skilled assistance in accidents and sudden illness and to prevent serious consequences before the arrival of the doctor or during transport.

The Order of the Hospital of St. John of Jerusalem has an old history, originating with the establishment of a hospital in Jerusalem in the third century A.D., when the healing art was under the influence of the church. Later, it became intimately associated with religious wars. In the latter half of the nineteenth century, the advent of scientific medicine weakened the control of the church on the one hand and witchcraft on the other, and placed the healing art on a new pedestal.

It was at the International Conference of the Red Cross Societies held at Berlin in 1869 that the real beginning of the ambulance movement was made after the Franco-Prussian War of 1870; when it had become apparent that ambulance work in war could not be properly done unless it was properly organized in time of peace. In 1877, the St. John Ambulance Association was formed with this new outlook, for which Queen Victoria granted a charter in 1888. What has been done for field hospitals by Florence Nightingale has been done for ambulance work by the St. John Ambulance Association. In 60 years, its powers and organization have developed

### Hæmatological values.

Sex	Locality	Number	Mean corpuscular volume	Standard deviation	Mean corpuscular hæmoglobin	Standard deviation	Mean corpuscular hæmoglobin concentration	Standard deviation	Authority
Male	Calcutta	30	90.49	± 7.90	28.53	± 2.31	31.07	± 1.20	Napier and Das Gupta, 1936.
"	Bombay	121	87.08 *	..	30.01 *	..	34.54 *	..	Sokhey <i>et al.</i> , 1937.
"	Assam	24	71.29	± 7.04	23.93	± 2.31	32.50	± 3.10	Napier and Das Gupta, 1936.
"	Cachar	25	84.93	± 10.78	25.14	± 3.70	29.72	± 2.94	Napier and Majumdar, 1938.
Unspecified	U.S. A.	..	87.00	..	27.5	..	35.00	..	Castle and Minot, 1936.
"	Britain	..	86.00	..	29.5	..	34.00	..	Whitby and Britton, 1939.
Females	Calcutta	128	86.82	± 7.28	27.42	± 2.89	31.57	± 1.76	Napier, 1939.
"	Bombay	101	88.53 *	..	29.06 *	..	32.86 *	..	Sokhey <i>et al.</i> , 1938.
"	Delhi	100	85.64 *	..	28.76 *	..	33.58 *	..	Benjamin, 1939.
"	Assam	20	77.30	± 7.70	24.50	± 3.00	31.20	± 1.70	Napier and Bilimoria, 1937.
"	Cachar	25	82.49	± 12.68	23.42	± 3.10	28.67	± 3.37	Napier and Majumdar, 1938.
"	Michigan	50	86.30	..	..	..	..	..	Bethel, 1936.
Pregnant females.	Calcutta	64	86.83	± 10.8	26.62	± 3.34	30.57	± 2.13	Napier <i>et al.</i> (unpublished).
"	Michigan	28	92.00	..	..	..	..	..	Bethel, 1936.

\* Calculated from data given, after applying factor  $\times 1.09$  to cell volume to allow for shrinkage, where this has not been done.

steadily throughout the British Empire and Dominions, so that India, Canada, South Africa, Australia, New Zealand and most of the colonies have now their own splendid organization and are training thousands of men and women in first aid and ambulance work, home nursing and air raid precautions and anti-gas measures.

In Jerusalem the Order still maintains its institution which is a well-equipped ophthalmic hospital and is doing useful work among the poor of all creeds who suffer from the scourage of ophthalmia in Palestine and the neighbouring countries.

The original emblem of the Order on its banner was a rectangular white cross on a red ground, the precursor of the Geneva Cross, the four arms of the cross being associated with the four cardinal virtues, *viz*, prudence, temperance, justice and fortitude. Later, in A.D. 1120 the statutes formed for its governance included an ordinance which enjoined that members of the Order should wear a white eight-pointed Maltese cross on their robes, the points representing the eight beatitudes—qualities—which sprang from the practice of the cardinal virtues. The practice of the English Grand Priory of the Order is always to depict the eight-pointed white cross on a black ground, the white being a sign of purity of heart and the black of poverty, as the Order is for 'Service for the poor and suffering' which is given gratuitously in charity. The Order took as its arms the white cross on a red ground which become a sign of mercy as its members wore a bright red garment in times of war. In time of peace they wore a black robe and thus the colour of the background was changed. Each of the eight points of the emblem has now a secular significance, representing the qualities which are essential for the skilled first aider. These qualities are observation, tact, resource, dexterity, sympathy, perseverance, discrimination, explicitness.



The eight-pointed ambulance cross.

This is all interesting history. Whether the present-day physician is religious minded or not it is an indisputable fact that 'if there is any possible way of increasing the wisdom and ability of mankind it must be sought in medicine' and organized medicine claims organized professional service. This service is not confined to the bedside or the operation table. The modern doctor, if his education does not stand on the basis of scholarship, mathematics, astronomy and history, has still, in the kaleidoscopic changes of world events, opportunities for gaining in general knowledge and giving a wider outlook to his profession. The medical man's humanitarianism, if it is no longer a sentimental overflow of the heart or a religious conviction, should be a demand of his intelligence. Nothing should be too insignificant nor regarded as below his consideration, much less the subject of first aid.

The ambulance work of the Order whose foundation is laid in peace time becomes spectacular and arresting in time of war. No didactic training in first aid need be given to the medical student, but first aid for the public forms a special branch which the qualified doctor should not treat lightly, if he has to give correct education to the public, as the first aid is also based on scientific knowledge. All the details of first aid for the public have been worked out by a panel of experienced doctors, after considerable scrutiny and examination. 'Pressure points' *per se* may not form an important part of *surgical anatomy*, but they have an important bearing on the arrest of bleeding in the hands of a first aider whose knowledge of *surface anatomy* can be only skin deep, but whose correct aid at the opportune time saves life. Occasions have arisen when failing respiration has had to be restored on the operation table, but the process of artificial respiration on an apparently drowned person on the river side would be a different matter. There are standard bandages for the use of a doctor in his surgery but it will be necessary to improvise a triangular cloth with its point, base and sides out of the handkerchief for a road-side accident, and there is a technique for folding and using this bandage too.

Many intriguing questions arise in the mind of the highly technical professional. Can he teach fractures without the use of x-ray plates or pathological specimens? Is a patient to be carried on the stretcher with his feet foremost while going uphill? Why is the primitive long Liston still the splint of choice for the fracture of the thigh bone and the Thomas splint relegated to an appendix in the first-aid book.

(Answer: Because the individual first aider can improvise only the former in emergency and the latter is reserved for trained squads.)

It will be seen that the problem of first aid forms a special branch of study and the St. John Ambulance Association has considered the subject from all its aspects, which is well worth the



attention of the doctor who is called upon to teach and examine a class. The work of the Ambulance Department of the Order does not end with the theoretical and practical teaching of first aid, home nursing, and air-raid precautions. It goes further and forms ambulance divisions of trained men and nursing divisions of trained women who are banded into uniformed and disciplined bodies for public service and who serve as auxiliaries to army medical and nursing services in time of war. Trained women who enrolled in the V. A. D. (Voluntary Aid Detachment) did useful work in the last war and they are enrolled now in the Voluntary Aid Service for nursing work. Trained men have formed ambulance corps. The Red Cross and the St. John Ambulance Association, the two recognized voluntary aid bodies in India, have formed a useful combination, the former taking up the financial responsibility and the latter providing personnel in whose training and practices the medical profession has ample opportunities for taking a conspicuous part.

The St. John Ambulance Brigade Overseas in India is in command of a chief commissioner at headquarters. There are fourteen brigade dis-

tricts for administrative purposes, eleven of which correspond to the geographical distribution of provinces, each being in charge of the head of its civil medical department; two brigade districts in charge of their chief medical officers correspond to a couple of the largest railway administrations and one is in a State. Ambulance divisions of uniformed men trained in first aid consisting of about twenty members and officers parade regularly to keep themselves in form. Similarly nursing divisions of uniformed women qualified in home nursing as well meet regularly to refresh their knowledge of nursing and form work-parties for the preparation of hospital comforts for the sick and wounded. Younger people in schools and colleges form cadet ambulance and cadet nursing divisions. The formation of these divisions is growing apace. Each division has its own medical officer designated the divisional surgeon who helps to maintain its technical ability. Members and officers are given various awards and badges of proficiency. Recognition is also given for service and the most deserving ones of any creed are admitted to the Order of St. John, which is a coveted honour.

## Medical News

### ADRENALINE PREPARATIONS SOLD IN INDIA

Quite a fair proportion of adrenaline chloride solution sold in India is below *par* in quality and sub-standard in strength.

This conclusion has been reached by the Biochemical Standardization Laboratory of the Government of India as a result of the study of 30 samples of adrenaline chloride solution (1 in 1,000 strength) which have been tested biologically for their purity and potency in the course of an all-India survey of the quality of drugs and medicinal chemicals undertaken by the laboratory.

Out of 30 samples analysed, as many as 12 (or 40 per cent) were markedly below strength (*i.e.*, less than 75 per cent in potency of a *known standard*). Amongst this lot, seven samples showed a strength of less than 50 per cent. Two samples apparently contained only about 10 per cent of an adrenaline-like blood-pressure-raising principle. Only nine samples (or 30 per cent) were found to agree with the potency claimed by the manufacturers.

The specimens were secured from practically all over India through the courtesy of the heads of medical administrations of the various provinces. Some were secured from the open market by the officers of the laboratory. Although the total number is small, the samples tested represent almost all the brands manufactured in India and abroad (England, Germany, France, Belgium, Switzerland), and available for sale in the Indian market.

The findings may therefore be considered as fairly representative of the conditions existing in this country so far as the quality of adrenaline solutions are concerned.

*Glass containers.*—The reasons for the poor quality of the solutions are being further investigated in the laboratory. In the form of a 1 in 1,000 solution in which it is usually offered to the public, adrenaline, unlike other drugs such as digitalis, ergot, etc., does not rapidly lose its strength in the temperature and humidity existing in India. In the presence of alkali,

however, adrenaline has been known to lose its strength, the deterioration being accompanied by a reddish or brownish discoloration.

Excess of alkali is sometimes present in the glass of certain containers (phials, ampoules, etc.) in which adrenaline has been found stored, and it is highly probable that this factor is at least partly responsible for the deterioration of the adrenaline solutions contained. Apart from a strict watch (by biological assay conducted by technical experts) on the quality of adrenaline powders from which solutions are made, manufacturers in India who are usually dependent on the supply of glass containers from outside, would, therefore, do well to test the alkalinity of glass containers before putting in solutions of adrenaline chloride.

*Gravity of the problem.*—The active principle of the medullary portions of the suprarenal glands, adrenaline is now one of the drugs in daily use in medical and surgical practice. Its most important actions consist of a constriction of the blood vessels with consequent rise of blood pressure, sometimes slowing of the heart, a direct stimulant effect on the heart muscle and relaxation of the bronchial muscles. In the prevention of local hæmorrhage, in local anæsthesia and in such conditions as shock, heart failure and asthma, adrenaline is extensively employed and is the mainstay of the physician and surgeon.

Adrenaline chloride solutions of very high strength or very poor quality may mean in some cases all the difference between the life and death of the patient. The necessity of a strict control of quality both in the interest of the patients to whom adrenaline is prescribed and of the doctor who expects results from his drugs is, therefore, apparent.

*Standardization.*—The standardization for the tests made in the laboratory was carried out by the accepted biological method of comparing the 'pressor effect' (blood pressure raising property) of an unknown solution with that of a *known standard* in a decerebrated



and pithed cat. This method of assay is difficult and requires considerable experience but if carefully conducted, it is capable of yielding results accurate to within 10 per cent of the standard.

A chemically-pure, natural, levo-rotatory brand of adrenaline powder with an optical rotation of  $-50^{\circ}$  to  $-53^{\circ}$  in a 4 per cent solution of the normal hydrochloric acid which was obtained from the British Drug Houses and certified by chemical and biological assay as up to proper standard, was used as the *reference standard*. Potency ranging between 90 to 110 per cent of the standard has been taken to be within the limits of allowable variation and has been declared as equivalent in potency to the reference standard. Samples not falling within this range have been declared as of poor quality and not suited for therapeutic use in the dosage ordinarily prescribed by physicians.

#### BIOCHEMICAL STANDARDIZATION LABORATORY (CALCUTTA).

#### CHOLERA VACCINES ON THE MARKET

How necessary it is that those who carry out inoculation against cholera with vaccine purchased in the open market, should have samples tested periodically to ensure that they are capable of giving protection and are sterile and safe for use, is revealed by a test lately made at the Central Research Institute, Kasauli. Certain samples of cholera vaccine manufactured commercially and supplied to a Public Health Department in India, were examined at the institute, and it was found that true cholera strains had not been used in the preparation. The sterility test also showed that the vaccines were contaminated and, therefore, not fit for use. It is possible that an appreciable number of commercially-produced vaccines on sale are of a similar type.

The value of inoculation against cholera is now generally recognized, but it is not sufficiently realized yet that, to be effective, the vaccine should be of good quality and be prepared from the genuine cholera organism. The view of the cholera advisory committee of the Indian Research Fund Association, which was accepted by the medical research conference, is that no protection against cholera can be expected from vaccine not prepared from strains of the true organism.

Recent research work, under the Indian Research Fund Association, has thrown new light on the nature of the cholera organism. It has been shown that there are many organisms in nature which resemble the cholera organism, but do not cause the disease.

To ensure that vaccine is made from the correct strains, it is desirable that strains tested and issued by certain specified laboratories, which have been continuously engaged in the study of the cholera vibrio should be used. The Directors of the Central Research Institute, Kasauli, the Calcutta School of Tropical Medicine and the King Institute, Guindy, have expressed their willingness to issue suitable strains to all laboratories, including those of commercial firms, for this purpose.

The cholera advisory committee have made certain recommendations on the technique of manufacture of cholera vaccine and the strains to be used, details of which may be had from the office of the Public Health Commissioner with the Government of India.

#### ANATOMICAL SOCIETY OF MADRAS

A MEETING of the members of the staff of the anatomy departments of the Madras Medical College and the Stanley Medical College was held in the Central Institute of Anatomy, Madras Medical College, on the 6th instant at 5 p.m. In the course of the meeting a scientific association—The Anatomical Society of Madras—was formed. Professor P. K. Koshy, B.A., M.B., F.R.C.P.(E.), was elected president, Dr. O. Nayinam, M.B., B.S., vice-president and Dr. U. V. Nayak, M.B., B.S., Ph.D. (Lond.), honorary treasurer and secretary.

#### PLANT PRODUCTS OF COMMERCIAL VALUE

Efforts were made throughout the year to secure specimens of medicinal plant products, plant materials used as vegetable insecticide, cereals, pulses, oil-seeds, commercial timbers, samples of hand-made and machine-made paper of different qualities, as are likely to be of public interest, says the annual report of the Botanical Survey of India for 1938-39.

The specimens collected have mostly been exhibited in the gallery of the industrial section of the Indian Museum, Calcutta. Cottage industries are a great centre of attraction to the visitors to the museum.

The different stages of the manufacture of paper are explained by charts, with finished products and raw materials, namely, bamboo, munj, ramsar, ulla grass, sabai or blabar grass and the various chemicals used. There are some exhibits which show how from ten pounds of bamboo treated with chemicals, one can have 4.2 pounds of finished paper. Samples of hand-made paper collected from Bengal, Nepal, Manipur, Kashmir, Bombay and Federated Shan States are on show. Some of the samples are strong enough to last over 1,000 years and are used for important and valuable documents.

#### DRUG EXHIBITS

Amongst the exhibits there are 25 well-known commercial drugs, namely, aconite, artemesia (kirmala), podophyllum (papra), taraxacum, colchicum, digitalis, belladonna, jurinea (dhup), rheum (revandehini), hyoscyamus (khorasani ajowan), valerian, etc., which were collected from Kashmir.

In a special show-case, with electric arrangements for illumination, is housed a set of commercial timbers from Dehra Dun with their magnified micro-photographic slides.

To increase their popular appeal, exhibits in the industrial section are being provided with new and up-to-date description labels and charts.

The industrial section has, in addition, been collecting information from various sources on many commercially important botanical products. Detailed information has been collected on hand-made paper, Kashmir drugs and vegetable insecticides and given publicity. Many correspondents in India and abroad have been supplied information on various economic plant products. Students and teachers, who visited the museum, were given all attention and help. Specimens were procured for and supplied to many scientific workers.

Over Rs. 3,00,000 was realized from the sale of Government of India quinine. The year opened with a stock of 112,564 pounds and closed with a balance of 97,071 pounds. The closing balance of bark was 256,106 pounds.

Distribution of quinine from Government of India stocks to the Punjab, North-West Frontier Province, Kashmir, Baluchistan and Ajmer-Merwara was restricted and the provinces were asked to make their own arrangements. With the end of the year, supply to the provinces, except the centrally-administered areas of Ajmer-Merwara and Baluchistan, was totally stopped.

In systematic botany some 2,000 plants specimens have been collected and added to the herbarium of the Royal Botanic Gardens, Sibpur. Nearly 3,000 specimens have been identified, for a large number of correspondents, the largest collections among those being from Sikkim, Baluchistan, Dehra Dun, Karachi and Burma. A large number of duplicate specimens has been distributed to several institutions in India and abroad and more than 3,000 sheets have been acquired in exchange, and about 4,000 sheets have been added to the herbarium.

The herbarium has been of considerable assistance to a number of distinguished botanists, both Indian and foreign, who came to visit and work in it for identification and confirmation of doubtful plant specimens of different localities. Mention may be made of the investigations on poisonous plants of India conducted by the assistants of Colonel Chopra for which all possible facilities and assistance were given.

## BENGAL COUNCIL OF MEDICAL REGISTRATION

*(Abstract of the Proceedings of the Council of Medical Registration, Bengal, at their meeting held on 17th January, 1939)*

THE term of members under clauses (f) and (g) of section 4 of the Bengal Medical Act, having expired, since the date of the last meeting, the following gentlemen were elected at the election held in the meantime:—

Dr. S. K. Mukherjee, D.O., D.O.M.S., F.R.C.S.

Dr. S. C. Sengupta, M.B., Ch.B., M.D., F.R.C.S.

Similarly the following gentlemen were elected under clause (f):—

Dr. Taraknath Ghosh, M.B.

Dr. Kalikinkar Sengupta, M.A., B.Sc., M.B., D.T.M.

Dr. Santoshkumar Chatterjee, M.B., F.R.C.S.

Dr. Basantakumar Ghosh, M.B., D.T.M.

2. The revised regulations for the Licentiate Examination, raising the course to 5 years and requiring I.Sc. as the preliminary qualification which were recommended in March 1937 were awaiting Government orders pending the views of the All-India Conference at Delhi on Medical School Education. The Council have proposed a deputation to wait on the Hon'ble Minister in charge to explain the urgency of the question.

3. The budget estimates for 1939-40 approved by the Council showed that against an expenditure of Rs. 14,535 the receipts from registration fee, etc., would amount to Rs. 8,250. The Council therefore needed a Government grant of Rs. 6,280 or at least Rs. 6,000, as against Rs. 4,500 hitherto taken as the normal grant. A loan of Rs. 2,000 taken from the Faculty in 1936-37 would still remain unpaid. At their previous meeting the Council had proposed to Government to receive a deputation from them to explain the financial position.

4. Dr. B. C. Ray, M.D., M.R.C.P., F.R.C.S., was elected as representative of the Medical Council, in the Bengal Nursing Council.

5. The following members were appointed to form the Penal and Ethical Cases Committee:—

(1) Lieut.-Col. T. C. Boyd, F.R.C.S., D.P.H., I.M.S.

(2) Dr. B. C. Ray, M.D., M.R.C.P., F.R.C.S.

(3) Dr. S. K. Mukherjee, D.O., D.O.M.S., F.R.C.S.

(4) Dr. J. C. Chatterjee, L.M.S.

(5) Dr. A. D. Mukherjee, L.M.F.

6. The following members were appointed for the School Inspection Committee:—

(1) Lieut.-Col. T. C. Boyd, F.R.C.S., D.P.H., I.M.S.

(2) Dr. S. K. Mukherjee, D.O., D.O.M.S., F.R.C.S.

(3) Dr. K. S. Ray, M.A., B.Sc., M.B., Ch.B.

(4) Dr. J. C. Chatterjee, L.M.S.

(5) Dr. A. D. Mukherjee, L.M.F.

7. The following members were appointed for the Examination (Faculty's) Inspection Committee on behalf of the Council:—

(1) Dr. S. K. Mukherjee, D.O., D.O.M.S., F.R.C.S.

(2) Lieut.-Col. B. G. Mallya, M.D., F.R.C.S., I.M.S.

8. The Council at their previous meeting had resolved that in the present conditions of the Ronaldshay Medical School (Burdwan) and Lytton Medical School (Mymensingh) their affiliation could not be continued further. Both are government schools, and on intimation from the Surgeon-General that action was being taken to remove the main defects, the Council extended the affiliation by one year, and in the meantime a further report from the inspection committee as to the progress made would be examined.

*(Abstract of the Proceedings of the Bengal Council of Medical Registration, at their meeting held on the 8th August, 1939)*

1. The Council considered that it was desirable that the country of qualification particularly when the qualification had been obtained from a foreign country should be mentioned along with the abbreviation used for medical qualifications, so that the public might not be misled and they expected that a convention

would be gradually established by registered medical practitioners if they follow this practice.

2. The Council decided that Government be moved to obtain legal opinion as to whether they could under the authority of section 18 (a) examine the medical qualifications of a foreign country which was not covered by the British Medical Acts.

3. Government Notification announcing the election of Dr. B. C. Ray, M.D., M.R.C.P., F.R.C.S., as a member of the Bengal Nursing Council was recorded.

4. The following resolution of the standing inspection committee was adopted:—

*Resolved*—that the committee recommend that no action should be taken for the inspection by them of medical schools outside Bengal; and that where any such institution desires to continue its recognition in Bengal, it should be sufficient that the institution is recognized by a Medical Council in any province in India, with which this Council has reciprocity of registration.

5. Lieut.-Col. J. C. De, I.M.S., was appointed a member of the standing inspection committee and the Penal and Ethical Cases Committee in place of Colonel Boyd, I.M.S., transferred.

6. The Council recorded the report by the registrar that Biseswar Das, a compounder who had given a medical certificate posing as a registered medical practitioner, had been prosecuted under section 29 of the Bengal Medical Act, 1914, and had been convicted and sentenced to pay a fine of Rs. 15 in default to undergo simple imprisonment for two weeks.

## POST-GRADUATE STUDY IN GREAT BRITAIN

WOMEN medical students and doctors who are planning post-graduate studies abroad are invited to correspond with the Chief Medical Officer, Women's Medical Service, Countess of Dufferin's Fund Office, Viceregal Estate, Simla (summer), Red Cross Building, New Delhi (winter), from whom advice can be obtained before leaving India about the various diplomas and courses of study available, the qualifications needed for each, and in general about facilities for residence and study abroad.

In England the services of the High Commissioner for India are available for similar advice.

Applications should be made to the High Commissioner's Education Department which is assisted in this matter, where necessary, by the Countess of Dufferin's Fund Medical Adviser in London.

Students are strongly advised not to leave India without assurance that they are qualified for admission to the examinations they intend to take.

(Sd.) G. STAPLETON,  
Chief Medical Officer, W. M. S.

## THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students are declared to have passed the D.T.M. Examination, Session 1939-40:—

### Passed

(Arranged in alphabetical order)

1. Ahmad Husain, M.B., B.S. (Punjab), private practitioner.
2. Anwar Ali, M.B. (Cal.), Assistant Surgeon, Government of Bengal.
3. Netai Charan Banerjee, M.B. (Cal.), private practitioner.
4. Amiya Ratan Basu, M.B. (Cal.), private practitioner.
5. Padma Nava Bose, M.B., B.S. (Punjab), private practitioner.
6. Amalendu Chakrabarty, M.M.F. (Cal.), private practitioner.
7. Biharilal Chaudhuri, M.B. (Cal.), private practitioner.
8. Pran Nath Chhuttani, M.B., B.S. (Punjab), private practitioner.

9. Ishwar Chander Chopra, L.R.C.P., M.R.C.S. (Lond.), private practitioner.
10. Barbara Guy Courtney, M.R.C.S. (Eng.), L.R.C.P. (Lond.), L.T.M. (Cal.), private practitioner.
11. Nirmal Chandra Das, L.M.P. (Assam), Assistant Medical Officer, Daisajan Tea Estate, Assam.
12. Nar Narain Dikshit, M.A., B.S. (Lucknow), private practitioner.
13. Jethalal Gordhandas Gandhi, L.C.P.S. (Bombay), private practitioner.
14. Santosh Kumar Ghosh, M.B. (Cal.), Clinical Assistant, Medical College Hospital, Calcutta.
15. Jyoti Prakash, L.M.P., L.C.P. & S. (Bombay), L.T.M. (Cal.), Pathologist, Civil Hospital, Ajmer.
16. Dinkar Ramrao Kaikini, M.B., B.S. (Bombay), private practitioner.
17. Sitaram Subrao Kulkarni, L.C.P.S. (Bombay), L.T.M. (Cal.), Medical Officer, P. G. Singhanee Hindu Hospital, Bombay.
18. Pallathucheryl Varkki Kurian, M.A., B.S. (Madras), private practitioner.
19. Md. Khaliler Rahman, L.M.P. (Assam), Assistant Pathologist, Berry-White Medical School, Dibrugarh, Assam.
20. Bhabesh Mukherji, M.B. (Cal.), private practitioner.
21. Mushtaq Ahmad Alavi, M.B., B.S. (Lucknow), private practitioner.
22. (Miss) Putli D. Nanavatty, M.B., B.S. (New Delhi), private practitioner.
23. Muhammad Azhar Noman, M.B., B.S. (Lucknow), Pathologist, King Edward VII Hospital, Benares City.
24. Dwijendra Lal Pakrasi, M.B. (Cal.), private practitioner.
25. Dhirubhai Kishorhbhai Patel, M.B., B.S. (Bombay), private practitioner.
26. Pabitra Kumar Paul, M.B., B.S. (Patna), private practitioner.
27. Umar Abdulla Pothiwala, M.B., B.S. (Bombay), private practitioner.
28. Braham Govind Prasad, M.B., B.S. (Lucknow), D.P.H. (Cal.), private practitioner—Awarded the 'Chuni Lal Bose' Gold Medal—1940.
29. Satya Pal Puri, M.B., B.S. (Punjab), private practitioner.
30. Suresh Chandra Ray, M.B., B.S. (Patna), private practitioner.
31. Upendra Chandra Sarker, M.B. (Cal.), Assistant Surgeon, Government of Bengal.
32. Satchidanand Subba Rao, M.B., B.S. (Bombay), private practitioner.
33. Kersasp Nuservanji Tankariwala, M.B., B.S. (Bombay), private practitioner.

## Current Topics

### The Sulphapyridine (M. & B. 693) Treatment of Pneumonia in Children

By C. H. SMITH, M.D.

and

R. L. NEMIR, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXIII, 18th November, 1939, p. 1857)

THE majority of the patients had lobar pneumonia (seventy-nine of the ninety-three), distributed from 2 months to 13 years of age. There were twenty-nine patients under 2 years with lobar pneumonia and fifty over 2 years. All of the eleven patients with bronchopneumonia were under 2 years of age.

Sulphapyridine was given by mouth, in most cases crushed and mixed with cereal, apple sauce or fruit juice. It was usually given shortly after a meal to minimize the possibility of nausea or vomiting. In the early cases 0.2 gm. per kilogramme of body-weight ( $1\frac{1}{2}$  grains per pound) was given on the first day, and half this amount on the subsequent days. We soon found that equally prompt defervescence was observed with three-fourths of this dosage in children over 2 years. The infants, however, seemed to require the original dosage, and this was continued for them. No child received more than 4.5 gm. a day, and the average total amount given to a child was 5.48 gm. The average total dosage for an infant under 2 years was 3.99 gm.

Half of the patients were treated for only two days and 75 per cent for not more than three days. The average duration of treatment was 2.6 days. It is our experience that if sulphapyridine affects the course of the pneumonia it does so within eighteen to thirty-six hours. In the first few cases treated it was given for from five to six days after the crisis, but the prompt fall of temperature after the drug is begun led us to shorten the time of administration. In the larger part of this series the drug was continued for only eighteen to twenty-four hours after the crisis. No definite recurrences of pneumonia have been noted. Five patients

had subsequent short rises of temperature, probably not true relapses of pneumonia.

Blood sulphapyridine determinations were done on many but not on all patients. The concentration was found to vary widely with the same dosage of drug, from less than 1 mg. to 12 mg. per hundred cubic centimetres. Three patients whose concentration was 0.8 mg. per hundred cubic centimetres had a crisis completed within eighteen hours after the drug was given. The average blood sulphapyridine determination was from 2 to 4 mg. per hundred cubic centimetres, and with this level in most cases prompt crisis was noted.

#### UNFAVOURABLE REACTIONS

The most frequent reaction was vomiting, usually of only one or two doses occurring in 15 per cent of the patients. This symptom was never severe enough to require stopping the drug. Vomiting can be greatly reduced by giving the sulphapyridine with food or directly after meals, a precaution which is often neglected in hospital practice. None of the patients became cyanotic from the drug, although several were cyanotic when it was first given. Extreme restlessness and delirium were observed in four patients, one of whom had a blood sulphapyridine concentration of 12 mg. per hundred cubic centimetres, the highest in our series. This baby had a peculiar agitated expression and constantly threw himself about. His extreme restlessness required the use of restraints to prevent falling out of bed. This agitated restlessness is not a part of any pneumonia picture. All four of these patients presented an alarming state; they had a peculiar intense pallor, although they were not anæmic. They were improved by sedatives (phenobarbital), by a large amount of fluids and by discontinuing the drug for one or two doses. Two of these babies were placed in oxygen tents without improvement of the nervous symptoms. A transient mild hæmaturia was observed in one patient. This child had received only 0.12 gm. per kilogramme of sulphapyridine; hæmaturia appeared on the third day of treatment and cleared within a few days. It must be pointed out that hæmaturia occasionally occurs in pneumonia without the use of

sulphapyridine. No other toxic symptoms were observed.

### RESULTS

The prompt and consistent precipitation of crisis following the oral administration of sulphapyridine has been reported by many observers, and our experience is no different. This reaction occurred within eighteen to twenty-four hours in sixty-nine of the seventy-nine patients with lobar pneumonia. Of course, it is possible that the drop in temperature of some of the patients coincided with the normal crisis, but such an explanation cannot account for all the reactions, particularly in those treated very early in the disease. Many of the patients treated on the eighth to the eleventh day were acutely ill with type XIV pneumonia, in which the average duration is from eight to fourteen days.

It has been stated that, although sulphapyridine provokes a crisis, the disease runs its course, and the consolidation does not resolve sooner than it would have done if untreated. This suggestion is contrary to our experience. The x-ray shadows and the physical signs begin to clear at once just as they do after a normal crisis.

The three patients with lobar pneumonia who failed to show the typical response to sulphapyridine were all infants under 2 years of age, all severely ill. It is possible that the sustained temperature in the first one of these patients was a febrile evidence of sulphapyridine intolerance or intoxication, since this baby had other signs of reaction, namely extreme restlessness, delirium, pallor and marked anorexia. His blood sulphapyridine determination was 12 mg. per hundred cubic centimetres. The second patient is remarkable only because he required forty-eight hours' therapy to produce a crisis. The third baby had pneumonia three times previously at Bellevue Hospital, some of these atypical pneumonia. We cannot explain his unusual reaction to sulphapyridine.

In five cases of lobar pneumonia, although the usual reaction occurred after sulphapyridine, secondary short febrile rises occurred. It has been suggested that the bacteriostatic action of sulphapyridine may produce improvement for a short time and then be followed by a relapse. There were only five patients whose temperature charts might be so interpreted. Only one of these cases clinically appeared like a pneumonia during the second temperature rise which yielded promptly to renewed treatment. The dosage of sulphapyridine was probably inadequate in case 5, but readministration of the drug was followed by prompt crisis. The other three patients had no new signs of pneumonia. One of these received no more drug, and the fever subsided just as promptly as in the cases in which it was given, so that it is not certain that any patients had true relapses. Short febrile episodes are often seen in hospital patients from insignificant causes. These three patients may all have had transient fever not associated with pneumonia. Roentgenograms in all five cases showed clearing pneumonias and no new consolidation. It is noteworthy that four of the five patients had pneumococcus type XIV pneumonia, a disease known for its severity. It is suggested also that the type XIV pneumonia may require a somewhat greater dosage than the other pneumococcal pneumonias.

In eleven cases of true broncho-pneumonia we have failed to observe the same dramatic, prompt response to sulphapyridine seen in cases of lobar pneumonia. The temperature of the patients with broncho-pneumonia remained elevated, and they seemed only slightly improved. Our series of this form of pneumonia this year is small, however. Four of the eleven patients died, approximately the average mortality rate for broncho-pneumonia during the past eight years. A much longer time will be needed to evaluate sulphapyridine therapy in this form of pneumonia. Kohn reports no effect on broncho-pneumonia in his experience at the Willard Parker Hospital.

One patient clinically thought to have broncho-pneumonia died and at autopsy was found to have lobular pneumonia, probably from aspiration. The walls of the bronchi were normal. This 6½ months old

baby was admitted to the hospital for a diarrhoea from which he was recovering when he developed pneumonia. Type XIX pneumococcus was found. The baby was treated promptly with sulphapyridine but died within thirty-six hours after the onset of the pneumonia.

There was one death among the seventy-nine patients with lobar pneumonia. This severely ill 16 months old baby died suddenly on the third day after admission to the hospital. A roentgenogram taken the day before death showed a pyopneumothorax (not diagnosed clinically), which was probably responsible for the death. No autopsy was obtained.

Only one patient developed empyema, an infant with type I lobar pneumonia. He developed physical signs, and a roentgenogram indicated suppurative pleurisy. On pleural tap 2 c.c. of thick pus was removed, from which type I pneumococcus was cultured. No further pus was ever found and the patient promptly recovered. This abortive course of empyema has been rarely encountered in our many years of observation of empyema, especially that following type I pneumonia.

Pneumococcal bacteremia was found in only one patient, a boy of 8 years, with type I lobar pneumonia. His defervescence occurred within eighteen hours in the typical manner. The drug was cut off after thirty-six hours, and the report of the blood stream invasion was obtained after the drug had been discontinued. Even with this small amount of therapy, the blood stream was sterile. As a precaution the drug was readministered for twenty-four hours, but all further blood cultures were sterile. *Streptococcus viridans* was found in two blood cultures from a patient with broncho-pneumonia. The blood cultures were sterile after several days' treatment with sulphapyridine, and the patient recovered.

### COMMENT

The consistent prompt crises observed in our patients with lobar pneumonia following the oral use of sulphapyridine is convincing to us that the drug is very efficacious in treating pneumococcal pneumonia (and perhaps also that due to the streptococcus). But the value of a therapeutic agent in pneumonia cannot be established in one season's time, since pneumococci are known to vary in their distribution and virulence from year to year. It may be that results will be less good in more serious epidemics.

In the present season we have had a lower percentage of type I pneumonia (10.9 per cent for the present year as compared to 17.8 per cent average for the past six years). There were probably more mild cases this season than usual, although many patients were very severely ill.

The failure of broncho-pneumonia to respond favourably to sulphapyridine may be explained on the basis of aetiology, since the bacteriology is variable and often no pneumococci are found. If a filtrable virus is the etiologic agent of broncho-pneumonia, as has been suggested by various workers and by some experimental work with animals, the explanation for the different reactions of these patients to the drug is probably indicated. Sulphapyridine has not been especially useful for diseases due to filtrable viruses.

For the older child sulphapyridine may well be the answer to the treatment of lobar pneumonia in the great majority of cases. In this age group (2 to 13 years) pneumonia is a milder disease with a much lower incidence of bacteremia and deaths than in adults. Even though the death rate in children may not be greatly affected, since it is already low, the shortening of the disease and the avoidance of complications justify the use of the drug. There may always be some patients who will require specific antipneumococcus serum therapy as well as the bacteriostatic agent sulphapyridine. Infants who are debilitated, chronically ill or anæmic and who may be unable to produce their own immune bodies may need specific serum as well as sulphapyridine. The necessity for obtaining a pneumococcus typing, preferably before chemotherapy is given, is clear. If sulphapyridine is not effective in the usual time, from eighteen to twenty-four hours, specific serum may be given without delay if typing



has already been done. In comparing results from different clinics with sulphapyridine in pneumonia, it is important to compare the results with reference to the types of pneumococci. It is known that the duration, severity and fatality of pneumonia is directly associated with the pneumococcus types.

We wish to reiterate that it is not necessary to continue sulphapyridine for many days in the fear of a relapse. In this series the drug was given only 2.6 days on an average. If the few early cases are excluded, this time drops to 2.3 days. The average total amount was 3.99 gm. for infants under 2 years and 5.48 gm. for patients 2 years of age and over. The largest amount given to any patient was 13.25 gm. The advice to try to stop the drug after 300-450 grains (20-30 gm.) have been given seems unwise in suggesting that these large amounts are usually needed. Sulphapyridine may be a poisonous drug in some cases, as is indicated by the reports of cyanosis, hæmaturia, leukopenia, delirium, liver damage and even death associated with the use of the drug. We believe that sulphapyridine should be given no longer than is necessary to effect a crisis and should be stopped very soon thereafter. To continue medication longer is unfair to the patient, just as it is with any drug having a cumulative poisonous action. The fact that we have observed no true relapses and have had no toxic symptoms of importance indicates the value of a wider trial of the small dose and short administration. Others have produced a crisis by one day's treatment and even by a single large dose.

#### RESULTS

1. From January to July 1939, ninety-three patients were treated with sulphapyridine; seventy-nine with lobar pneumonia, eleven with broncho-pneumonia, one with lobular pneumonia and two whose pneumonia was classified as 'subacute pneumonia'.

2. In broncho-pneumonia there was no apparent effect on the course in any of the eleven patients, four of whom did not survive.

3. In uncomplicated lobar pneumonia with small dosage, for two or three days only, a crisis occurred within eighteen to twenty-four hours in seventy-four of the seventy-nine cases. In the five other cases crisis occurred in forty-eight hours. One death occurred from pyopneumothorax. The short duration of therapy is emphasized not only because of its success but also because of the very few untoward reactions observed.

### Canned Foods in Relation to Health

By SIR WILLIAM SAVAGE, B.Sc., M.D. (Lond.)  
(Abstracted from the *Lancet*, Vol. II, 4th November, 1939, p. 991)

#### NUTRITIVE PROPERTIES

REDUCED to essentials, the canning process involves preliminary treatment to select the parts of the food which are suitable for canning and in some instances to blanch, soften, or otherwise prepare the food and a subsequent heat treatment in sealed containers to render the food safe for storage for long periods and subsequent usage after preparation. All canned foods are therefore subjected to treatment, particularly by heat, and it is possible that this may affect the nutritive qualities of the food so treated.

On the quantitative side there is no evidence that foods so treated have their total nutritive value affected in any way. Indeed from this point of view they possess considerable advantages due, on the one hand, to the fact that to give a successful commercial product the foods must be utilized by the canner in an extreme state of freshness and, on the other hand, that the preliminary treatment is calculated to make the whole of the food canned available as food without any wastage.

Qualitatively the position is not quite so simple, for theoretically it is possible that the treatment given might affect the mineral balance and the vitamin

content. The question of mineral balance really only arises as regards milk, and there is no evidence that it is affected. Henry and others, who studied this and other questions for dried and evaporated milk, state 'no significant difference was found between the biological values of the proteins (nitrogen) of the processed milks', and 'as regards biological value and true digestibility the figures show very slight reduction but not of statistical significance'.

Our knowledge of vitamins and the conditions under which they are destroyed or reduced in foods has been greatly augmented in recent years, so it is now possible to furnish reliable data as regards their presence in canned foods.

**Vitamin A.**—Both this vitamin and carotene are insoluble in water and stable even at high temperatures, provided there is an absence of oxygen. Vitamin A is much more sensitive to oxidation than to the degree of heat. Experimental work confirms that canning is not destructive to this vitamin and is definitely less prejudicial than ordinary cooking.

**Vitamin-B<sub>2</sub> complex** is very heat stable; but, since it is water soluble, loss is to be anticipated from the preliminary washing (for fruits and vegetables); but this applies even more so to ordinary cooking. The experimental work done is not very large; but as regards riboflavin, probably the least stable member of the complex, no loss has been observed in several foods, including evaporated milk.

**Vitamin D** has a high stability to heat, and experimental work confirms that no destruction takes place during canning.

**Vitamin B<sub>1</sub>** is comparatively little affected by oxidation and possesses considerable resistance to heat in an ordinary acid medium. On the other hand, it is water soluble. Preparation processes, whether for ordinary domestic cooking or for canning, may cause considerable loss of this vitamin. Roscoe found that about half the B<sub>1</sub> content of spinach went into solution in the cooking-water during a period of 15 minutes' boiling, and Baker and Wright show considerable cooking loss with some foods. Apart from loss in preparation the rather scanty experimental evidence suggests that the destruction of vitamin B<sub>1</sub> in the canning is usually small, but that there is some. Except for milk, there do not appear to be any reliable comparative figures of the vitamin-B<sub>1</sub> content of the same food before and after canning. For milk Henry found little or no destruction with dried milks but considerable loss with evaporated milk.

**Vitamin C** is readily affected by heat, by washing, and by storage. Numerous investigations have been made on the influence of these factors, particularly as regards ordinary cooking. The vitamin-C content of fruits and vegetables shows considerable variations even with the same food. Further, the content begins to diminish from the time of picking, and here canned foods have a definite advantage as economic factors necessitate the shortest possible time between picking and canning.

Very few papers give comparative figures for the vitamin-C content of the same foods raw, cooked, and canned. Valuable studies have, however, been made by Oliver; she concluded:—

'Part of the vitamin C content is extracted from plant tissue when it is heated in liquid as in cooking and canning. At the end of the normal process in each method the ascorbic acid is frequently evenly distributed throughout solid and liquid. The percentage of ascorbic acid destroyed in both cooking and canning is comparatively small, but considerable quantities are lost to the consumer when the water used for cooking vegetables is discarded. Vegetables after storage may contain appreciably less vitamin C than the fresh material after canning. . . . The ascorbic acid content in canned material tends to fall on storage, but for all practical purposes the loss is not great.'

The much higher content of ascorbic acid in raw fruits and vegetables is shown in the table below.

Henry and others experimenting with evaporated milk, found a loss of 30 per cent of vitamin C. Numerous other examinations of canned fruits and

orally indicates that it may frequently be adapted for self-administration. This form of therapy is certainly not advisable except for intelligent, co-operative patients. Forgotten doses of medication or negligent behaviour on the part of the patient must inevitably lead to relapse with consequent possibilities of infection of other people. It is essential that the patient take the medication regularly, as directed by the physician, or that the physician insist on the intramuscular route for therapy for unco-operative patients.

There are, of course, certain instances in which the oral route of medication would be a valuable adjunct in syphilis therapy. It can be used with caution for those individuals whose business or profession necessitates occasional absences from the physician's supervision. It should prove useful for those rare persons who have unusual difficulty in taking intramuscular injections because of resultant pain and induration of the muscles. It is also possible that in selected cases of congenital syphilis and in some cases of cardiovascular and latent syphilis the oral route of medication would be distinctly useful.

In the course of experiments directed toward the utilization of sodium bismuthate in antisyphilitic therapy, Hanzlik, at Stanford University, evolved preparations resulting from the interaction of sodium bismuthate, tri-isopropanolamine and propylene glycol, known as sobisminol mass and sobisminol solution. These products have been before the Council on Pharmacy and Chemistry for approximately three years, a period which was necessary for the accumulation and proper evaluation of evidence for the efficacy of the orally administered product. The studies of Hanzlik and his co-workers, of Sollmann, Cole and Henderson, and of others have shown, by clinical observations of antisyphilitic effects of sobisminol mass when given in sufficient dosage, that there is satisfactory absorption of bismuth following sobisminol mass by the oral route. Attention is directed to a rapid clinical method for quantitative determination of bismuth, devised by Hanzlik and his co-workers, which has been used effectively to maintain accurate observations of the level of bismuth excreted in the urine of patients with bismuth preparations. Adequate references to these studies appear in the report of the Council on Sobisminol. While some gastro-intestinal disturbances have been encountered, generally they have not been sufficiently serious to interfere with adequate treatment.

This oral remedy cannot be expected to replace completely the carefully supervised use of other established therapeutic agents. It is to be emphasized that, while an oral bismuth preparation may in some situations be substituted in whole or in part for a bismuth preparation administered intramuscularly, it could never serve as an adequate substitute for alternate courses of arsenicals and bismuth compounds.

Sobisminol mass must not be sold over the counter to the public as a cure for syphilis. If it were thus marketed, the product would be a real danger and detriment to the public health. Both Hanzlik and the manufacturers are most anxious that no such contingency shall arise. Therefore, according to agreements between the board of trustees of Stanford University and each of the three firms already licensed to manufacture the product, every legal effort is being made to prevent the sale of capsules of sobisminol mass to the public other than on or by the prescription of the physician. Self-medication in acute syphilis can only lead to relapse and resultant danger to the public health.

The ultimate evaluation of the therapeutic efficacy of a new drug such as sobisminol mass necessarily requires a long time. The close co-operation of Hanzlik and other investigators, the manufacturers, the Food and Drug Administration and the Council on Pharmacy and Chemistry in careful studies designed to evaluate and control this new product properly is highly commendable.

To summarize: A new antisyphilitic agent with the special property of effective oral administration will soon be taking its place in the alleviation of the

ravages of syphilis. Physicians, pharmacists and public health authorities must take care that sobisminol mass is not supplied directly to the public. Such distribution would obviously result in inadequate treatment of unrecorded and uncontrolled cases and thus would become a serious menace both to the individual and to the public health. Lastly it is pointed out that oral administration of bismuth compounds is not intended to replace the generally accepted use of bismuth preparations intramuscularly, except where special conditions prevail.

### Collapse Therapy for Pulmonary Tuberculosis as a Public Health Measure

(From the *Journal of the American Medical Association*, Vol. CXIII, 16th December, 1939, p. 2241)

SINCE the late Theodore B. Sachs called attention to the menace of the wide spread of tuberculosis in Chicago, the isolation of patients with the disease in the open, or contagious, stage has come to be considered the important feature in the campaign against this disease. Isolation of patients with tuberculosis in a contagious form from children under 16 years of age was made mandatory in 1917. Despite the energetic and even rigorous enforcement of the law, the number of uncontrolled cases of tuberculosis in the community was not decreased. Hruby stated that in 1931 there were 700 patients on the waiting list of the Municipal Tuberculosis Sanitarium and as many on the waiting lists of the Cook County Hospital and Oak Forest institution. There were 20,000 registered cases in Chicago but only 2,471 available beds. While the idea of isolating patients with open tuberculosis was correct, it failed in its practical application for the simple reason that there was no place for the isolated persons to go.

In 1931 the board of the Municipal Tuberculosis Sanitarium initiated a programme of collapse therapy on a mass scale in an attempt to stem the sources of infection. Every suitable patient at the institution and in the field was to receive the benefits of collapse therapy. The results of the campaign have now been analysed. Of 7,344 patients treated during the period between 1931 and 1936, 3,090 were treated by the induction and maintenance of pneumothorax for more than three months, while 3,584 patients were treated without collapse therapy. Of the 3,090 patients treated, 94.2 per cent had advanced tuberculosis, 84.4 per cent had positive sputum and 81.3 per cent had cavities. Of the total, 14.2 per cent were Negroes. In the collapse group 53.9 per cent were converted from positive sputum to negative, while in the control group the conversion amounted to 15.3 per cent. Thus, since the inception of the programme, according to Hruby, 1,285 'fountains of infection' have been shut off. After the treatment 64.3 per cent are still living, as compared with 31.3 per cent in the control group. Of 1,215 patients with positive sputum converted to negative, 227 had been negative from two to three years, 154 for from three to four years, 94 for from four to five years, 27 for from five to six years, and 25 for six years and over. While the mortality rates for the Municipal Tuberculosis Sanitarium based on a study of 8,779 cases amounted to 82.96 per cent for a five-year period and 91.6 per cent for the ten-year period, the group in which collapse therapy was practised showed a survival rate of 69.3 per cent at the end of five years.

Extensive collapse therapy justified itself from the point of view of protecting the community, because it converted a relatively large number of open cases, for which hospitalization facilities did not exist, from a positive to a negative sputum. To overstress the importance of the widest possible collapse programme and at the same time to understress or to leave unemphasized the much greater importance of creating facilities for the immediate hospitalization of the tuberculous would be wrong. A more correct orientation toward the pneumothorax therapy would be to regard it as a problem of the individual rather than as a public health measure. Indirectly of course the public



would benefit as well. In every urban community there are many persons with unrecognized open tuberculosis. Cases are diagnosed as a rule in the advanced stage of the disease, that is, after countless numbers of others have been exposed to infection. Not all the cases are suitable for collapse therapy and the latter is effective in only a certain proportion. Pneumothorax therapy cannot therefore be regarded as more than a significant aid in the wider problem of the eradication of tuberculosis. The control of this condition is largely a matter of early diagnosis and segregation. No doubt the programme would have yielded still better results in Chicago if better facilities for applying the principle of segregation had been available.

## Clinical Studies in Non-Dysenteric Intestinal Amœbiasis

By J. J. SAPERO

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XIX, November 1939, p. 497)

DIVERSE opinions are held regarding the pathogenic rôle of *Entamoeba histolytica* in cases of intestinal amœbiasis which present neither a present nor past history of dysentery. Certain clinicians tend to attach clinical significance only to the dysenteric manifestations of the organism; others attribute to *E. histolytica* a wide range of protean symptomatology. Although the view-points of the majority are at neither of these two extremes, there is a considerable lack of agreement as regards both the nature and the frequency of symptoms in amœbic infections and their clinical importance when dysentery is absent.

Dobell in his monograph states that probably less than 10 per cent of persons who become infected with *E. histolytica* ever suffer to any appreciable extent from their parasitism. Faust believes that 90 to 95 per cent of persons harbouring the organism are apparently symptomless carriers. More recently, Wenrich, Stabler, and Arneith noted little evidence of pathogenicity in carriers found in an examination of college students, and observed that a control group seemed to have as many or more signs of ill health than those in their series who were carriers of *E. histolytica*.

Findings contrary to these have been reported by other workers. Craig, who has had wide experience in clinical amœbiasis, states that in his experience about 65 per cent of carriers have had symptoms referable to their infection, and that these symptoms disappeared after the eradication of the parasite. Philpitschenko reports that one-half of 400 apparently healthy carriers found in a survey of Leningrad food handlers had various intestinal disorders. Johnstone and his co-workers found that 52 out of 92 infections among a prison group were associated with notable gastro-intestinal upsets.

In addition to the discrepancies in the frequency with which symptomatology is associated with *E. histolytica* infections, it is to be noted that agreement is also lacking regarding the nature of the symptoms. Certain observers have incriminated the organism as the causative agent of symptoms far remote from the gastro-intestinal tract. Boyers, in an analysis of 1,961 complaints presented by persons found to be infected, believes his results show symptomatology referable to many other systems of the body. Craig, although mainly emphasizing the gastro-intestinal manifestations, notes that frequently nervous and circulatory disorders are attributed to *E. histolytica*. Arthritis, iritis, Hodgkin's disease and other conditions have been suspected of being caused by the organism, but no convincing ætiological relationship has been demonstrated in such cases and those claims have not at present gained any acceptance.

Many features lend particular importance to the problem of non-dysenteric amœbic infections. Primarily to be considered is the concept that *E. histolytica* is an obligate tissue parasite and that in every individual harbouring the organism there is a process of invasion

and repair accompanied by more or less injury, the amount of disease, in all probability, being dependent on host resistance. As reliable estimates place the incidence of the organism to be about 10 per cent in the United States, it becomes important to reach some agreement on what proportion of the cases of amœbiasis show evidence of injury.

**Physical signs.**—One of the most striking findings was the presence of abdominal tenderness. No less than 29 out of 46 gave this sign. The most prominent localization was at McBurney's point. In several instances this sign was so marked that had the individual complained concurrently of the symptoms encountered in appendicitis, operation would have appeared advisable. Circulatory abnormalities were not observed.

**Nature of symptoms.**—An analysis was made of 47 cases in which there was no ætiological factor other than the parasitic infection which would adequately explain the syndrome. To these were added seven cases in the control group who, although admitted for treatment for some unrelated condition, were found to be suffering concurrently with symptoms referable to their *E. histolytica* infections.

TABLE

Subjective complaints and objective signs in 54 hospital cases harbouring *E. histolytica* in which no other ætiological factor would adequately explain the syndrome.

### Past history—

Dysentery	..	..	..	0
Appendicitis	• ..	..	..	24

### Present history—

Nausea	..	..	..	20
Vomiting	..	..	..	6
Distension or flatulence	..	..	..	18
Heart-burn	..	..	..	12
Abdominal pain	..	..	..	50
Epigastric	..	..	..	13
Umbilical	..	..	..	9
Right lower quadrant	..	..	..	14
Left lower quadrant	..	..	..	5
Generalized	..	..	..	9
Bowel movements, normal	..	..	..	28
Bowel movements, abnormal	..	..	..	26
Diarrhœa	..	..	..	9
Constipation	..	..	..	12
Diarrhœa and constipation	..	..	..	5
Headaches	..	..	..	16
Fatigability	..	..	..	14
Nervousness	..	..	..	10
Loss of weight	..	..	..	7

### Physical signs—

Tenderness, abdominal	..	..	..	37
Epigastric	..	..	..	7
Cæcum	..	..	..	18
Ascending colon	..	..	..	7
Transverse colon	..	..	..	8
Descending colon or sigmoid	..	..	..	10

Almost one-half had at some recent time come under observation for appendicitis. Occasionally, upper gastro-intestinal complaints occurred to the exclusion of all other complaints. Pain was the most frequent symptom. The bowel movements were normal in over one-half of the cases. Constipation was a more frequent complaint than diarrhœa, this latter symptom occurring in but a small proportion of the cases. Nervous and circulatory disorders occurred but almost always in association with and subordinate to the gastro-intestinal complaints. Tenderness in various regions of the colon was elicited in 37 of the 54 cases and again the sign was commonly localized over the cæcum.

TABLE

Tentative admission diagnoses on 47 cases in which later clinical study revealed no adequate cause to explain the syndrome other than the presence of *Entamoeba histolytica*.

	Number of cases
Appendicitis, subacute or chronic ..	18
Peptic ulcer or chronic gastritis ..	10
Enteritis, chronic ..	7
Gall-bladder disease ..	4
Gastro-enteritis, acute ..	3
Appendicitis, acute ..	3
Renal colic ..	2
TOTAL ..	47

The tentative admission diagnoses made in 47 cases demonstrate the wide variation of conditions simulated by amoebic infections. The large number of cases thought to be appendicitis is consistent with other observations recorded in this series. Of those cases which came to operation, only those were included in which the pathological report of the appendix revealed no evidence of disease. It is to be noted that the larger number of cases were considered subacute or chronic manifestations of appendicitis, most of which were discharged without operation.

The most frequent was pain, being presented by 34 out of 47 cases. In three of the cases the complaint was mainly of weakness and in one the chief symptom noted by the patient was headache.

TABLE

Chief complaint in 47 cases harbouring *Entamoeba histolytica* in which there was no adequate cause to explain the syndrome other than the presence of the organism.

Pain ..	34
Epigastric ..	11
Umbilical ..	5
Right lower quadrant ..	8
Generalized ..	8
Lumbar ..	2
Nausea ..	1
Constipation ..	4
Diarrhoea ..	3
Alternating constipation and diarrhoea ..	1
Headache ..	1
Weakness ..	3

**Result of treatment.**—Carbarsone in 0.25 gram capsules administered twice daily for a period of 10 days was given as a routine. The follow-up examinations were made between six and twelve months after treatment. Approximately three-fourths obtained relief following carbarsone administration. Although but few cases are included in which no treatment was given, it is of interest that the results were exactly opposite, the majority stating either that their symptoms had persisted or had become aggravated.

**Comment.**—Judging from the rarity with which diagnoses of non-dysenteric phases of amoebiasis are made in medical practice, and considering the prevalence, of *E. histolytica*, one would come to the conclusion that clinical manifestations of the organism without dysentery are rarely of such severity as to require medical assistance. In the present investigation, however, quite the contrary proved to be so. Even in what may be presumed to be a highly resistant group, some of the infected individuals presented complaints which could not be regarded as unimportant. In the hospital study an impressive number of cases proved to be of amoebic origin and had not the presence of the parasite been demonstrated, the final diagnoses in these cases would have fallen in that large and unsatisfactory group in which neither the true cause nor the nature of the disorder is known.

The most striking feature of the cases studied in the investigation was the dissimilarity of their clinical manifestations as compared to the symptomatology

encountered in amoebic dysentery. Whereas the presence of dysentery, or blood and mucus in the stools immediately brings to mind the possibility of an amoebic process, the same organism is capable of producing disorders which give but scant clues to the nature of the disease. This observation becomes of greater importance in view of the fact that the largest proportion of amoebic infections are of this latter type. This was demonstrated in a recent Naval survey in which only 4.6 cases of dysentery were found for each 1,000 individuals harbouring *E. histolytica*. Thus despite the less serious nature of the non-dysenteric cases of intestinal amoebiasis as compared with those presenting dysentery, the difficulties in their diagnosis and their prevalence constitute a problem of some importance in clinical medicine.

It appears that a large number of apparently obscure gastro-intestinal cases which seek relief in hospitals and clinics are actually cases of amoebiasis and that frequently these cases are not being diagnosed. The lack of recognition of the non-dysenteric syndromes is due to the fact that a positive diagnosis is dependent on the demonstration of the organism in the stool examination. It is known that rarely should the organism be reported in any less than 5 per cent of routine stool examinations, yet too often hospital laboratory reports fail to reveal any such incidence of infection. Where this is so, the infections cannot be diagnosed and this situation has led to a false impression regarding the clinical importance of non-dysenteric manifestations of *E. histolytica*.

Certain clinical aspects of these cases are characteristic enough to bring to mind the possibility of an amoebic infection and lead to an intensive search for the parasite by stool examination. From the clinician's standpoint, a clear understanding that blood and mucus need not be associated with amoebic infections is of fundamental importance. Usually the non-dysenteric case is first suspected of being some well-defined and common gastro-intestinal entity, but a study shows so much to be atypical that the anticipated diagnosis cannot be reached. It is this very atypicalness which should suggest amoebiasis, and with abdominal pain as a prominent complaint, and when the symptoms are characterized by chronicity and recurrency, these features all become especially suggestive of amoebiasis.

Of special interest in the present investigation was the common occurrence of a syndrome simulating subacute or chronic appendicitis. Appendicitis was particularly apt to come under consideration in the disorders encountered in these groups, but the frequency with which the various attending physicians were led to consider the possibility of disease of the appendix was a striking feature of the investigation and one which indicated the organism to have an important rôle in such syndromes. The possibility of a large proportion of the non-dysenteric cases suffering from an amoebic typhlitis suggests itself. Many of the cases harbouring the organism were subjected to operation. In none of the infections were ill effects noted as a result of operation, and in a few, serious results undoubtedly would have followed had operation been withheld. The significant fact was that in many cases the signs were too mild to indicate surgery, while in others there was a return of like symptoms after operation, these facts suggesting the advisability of anti-amoebic therapy in connection with other indicated treatment in these cases.

**Summary.**—In the present clinical investigation only cases of intestinal amoebiasis in which there was neither a present nor a past history of dysentery were studied. The cases comprised both symptomless carriers of *E. histolytica* and infected individuals with complaints of varying severity. Control observations were made whenever feasible. Only those symptoms and signs were ascribed to *E. histolytica* after other possible causes had been ruled out. In all, 216 cases of non-dysenteric amoebiasis were studied, of which 100 were found to have symptoms.

1. A study of the occurrence of symptomatology in a selected group of 106 apparently healthy men harbouring *E. histolytica* showed 46 or 43.4 per cent to have

symptoms. A control group of 108 cases negative for intestinal protozoa revealed but 8 or 7.4 per cent to have complaints. Of the 106 cases of amœbiasis only 13.2 per cent of the complaints were of any appreciable severity.

2. Of 236 individuals harbouring various intestinal protozoal species, but not *E. histolytica*, the percentage with symptoms was similar to that found in the non-parasitized group, with the exception of *Dientamoeba fragilis* in which 27.3 per cent of 44 cases presented symptoms. Similarly, some of the flagellates presented higher percentages than the controls. An explanation of this apparent pathogenicity was offered.

3. A study of the blood findings in 61 cases of apparently healthy carriers of *E. histolytica* showed no significant differences from the results obtained in a control group of an equal number of individuals not harbouring the parasite.

4. Despite the apparent trivial nature of the complaints presented by most of the cases in an ambulatory group, it was found by a study of various hospitalized groups that a considerable number of non-dysenteric amœbic infections are severe enough to require hospitalization. In 47 such cases the disease picture was so obscure that only the finding of the parasite in the stool led to the proper diagnosis, and in these, specific anti-amœbic treatment gave good results where other methods had failed.

5. A study of the nature of complaints revealed these to be primarily referable to the gastro-intestinal tract, yet without blood and mucus in the stools and usually without bowel abnormalities which might suggest an amœbic process. Complaints referable to both upper and lower gastro-intestinal tracts appeared with equal frequency. Complaints referable to other systems were seldom encountered. Chronicity, recurrence and mildness of the symptoms were characteristic features.

6. A symptom-complex simulating subacute or chronic appendicitis was the most commonly observed syndrome in this series of non-dysenteric cases of amœbiasis.

### Treatment of Gastric Ulcer

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(Abstracted from the *Medical Press and Circular*, Vol. CCIII, 14th February, 1940, p. 132)

It is impossible in a short paper to attempt a complete review of so wide a subject, or to avoid being rather dogmatic. Some preliminary important essentials are not controversial. Accurate diagnosis must precede treatment, and this can only be made, after the ulcer is suspected, by full investigation (x-ray by an expert, repeated examination of stools, fractional test meals, possible gastroscopy, possible surgery). Most peptic ulcer cases have dyspepsia, but not all; presenting symptoms may be (a) anæmia, from long continued slight blood loss; (b) sudden gross hæmorrhage (which may be concealed); (c) perforation, with local or general peritonitis. Provided the diagnosis has been made as completely as possible, and is reviewed as fully if treatment does not restore the patient to complete health, the general practitioner is as capable as anyone of carrying out that treatment if conditions at the patient's house are relatively good. He is certainly never justified in treating a case without such investigation.

I have previously emphasized the difference in prognosis, treatment and probably ætiology between gastric and duodenal ulcer: subsequent work has made this differentiation even more important. Duodenal ulcer is probably never the site of subsequent carcinoma. Finsterer, of Vienna, finds an incidence of at least 15 per cent of carcinoma in the histology of chronic gastric ulcers resected. Duodenal ulcer occurs at an earlier age, and for every woman with a duodenal ulcer there are nine men, while the incidence of gastric ulcer is approximately equal in the two sexes. Perforation is nine times more common in men than in women,

and is far more common in duodenal ulcer than in gastric. Duodenal ulcer has no special social incidence; its ætiology is unknown, but neurosis is very commonly associated with it. Gastric ulcer is predominantly a disease of poverty, is known to be associated with the gastritis which occur in serious infections (e.g., diphtheria) in childhood and adolescence, and there is no obvious association with anxiety.

There is some evidence that the relative incidence of duodenal and gastric ulcer varies according to the country; in the U. S. A. duodenal ulcer appears to be more common than gastric; in England gastric ulcer is quite as common as duodenal. It is supposed that the proportion in Scotland is approximately the same as in the U. S. A., and this is borne out by my own experience in the Highlands for the last twelve months, during which I have seen 19 proved cases of duodenal ulcer, but only 11 cases of gastric ulcer and one case of proved ulcer carcinoma. Mr. A. J. C. Hamilton informs me that in approximately the same period his surgical experience at the Royal Northern Infirmary and in private practice included 23 cases of duodenal ulcer and seven gastric. Perforation tends to increase the proportion of duodenal to gastric cases seen in surgical practice, and the economic status of the patients undoubtedly affects the incidence in published series of cases.

These facts, which have a definite bearing on prognosis and treatment, are of little or no help in diagnosis: one is never justified in assuming on clinical evidence alone, no matter how 'typical' the symptomatology that a given patient, whatever his age, class, or sex, has one or the other. At the risk of becoming tedious I wish to repeat that it is thoroughly bad practice, involving the taking of quite unjustifiable risk, to treat any case with more than a history of a week or two as one of 'indigestion' or as gastric or duodenal ulcer without full investigation of the site and chronicity of the ulcer. Disappearance of symptoms under treatment is no sure guide to healing; cancer cases will often 'improve' under the same conditions.

To put the position shortly: there is almost complete ignorance as to the cause of duodenal ulcer, and treatment is therefore extremely unsatisfactory, with a high relapse rate and high perforation rate; it only kills, however, through perforation, massive hæmorrhage, or pyloric stenosis from scarring. Ulcers on the proximal side of the pylorus may be found at any age, but are commoner in middle and old age; even with present knowledge it is probably a preventable disease (well balanced diet, avoidance of grave infections—especially in childhood). The risk to life from gastric ulcer is mainly from profuse bleeding (mortality low with good treatment, 30 per cent under the old starvation-rectal saline regime), and from the development of carcinoma on the site of a chronic ulcer. Treatment is extremely satisfactory, except when chronicity makes the risk of cancer great enough for surgery to be necessary. Finsterer, the king of gastrectomists, has a direct mortality in simple ulcer resections of 2 per cent; for most surgeons undertaking the operation it is at least 10 per cent. Finsterer's mortality for gastrectomy in cases thought to be simple ulcer, but subsequently shown by careful histology to have undergone malignant change, is 4 per cent when other organs are not involved, 33 per cent when they are; his five-year survival rate for all cases of ulcer-cancer is only 9 per cent.

It is essential to bear these points in mind when deciding on the line of treatment to be followed on a given case. I would add three other cautions:

(a) If a patient with supposedly simple non-perforating ulcer of the stomach continues to get pain after resting a week in bed, the diagnosis is wrong.

(b) Ninety-six per cent of simple ulcers are near the lesser curvature, the remaining 4 per cent in the prepyloric area. A greater curvature ulcer is malignant.

(c) Free hydrochloric acid is frequently present after carcinoma has appeared.

## OUTLINE OF TREATMENT IN GASTRIC ULCER

(A) *The patient is not cachectic, has not had any gross hæmorrhage, and the ulcer has been shown by x-rays to be near the lesser curvature or prepyloric.*

(i) Success will largely depend upon the length of time which the patient can spend in bed, and upon his subsequent ability to take a liberal diet of the right composition. Alkalis and antispasmodics play no part in the treatment. They may relieve pain, but will never heal the ulcer; rest and good diet will do both. Gastric ulcer is seldom associated with hyperchlorhydria; a low acid curve is common, and achlorhydria not rare. Alkalosis during treatment with large doses of alkali is a real danger and occasionally fatal.

The longer the history, the longer the rest required. The patient with a few weeks' or months' history needs at least one month in bed and a further two months' freedom from any heavy work. Several years of history means several months of bed treatment, complete for some weeks, and thereafter for at least 18 hours out of the 24. Since there is no absolute criterion of complete healing (with the possible exception of gastroscopy—neither x-ray appearances nor the absence of blood in the stools is a guarantee), one must insist on treatment for some weeks after apparent healing has occurred as judged by the radiologist.

Since chronic ulcer is more common among men than women, difficulty is sure to be encountered in persuading patients to undergo such a long period of unspectacular treatment unless the position is fully explained, the risks emphasized and full consent obtained at the outset; the difficulties are exactly those encountered in advising patients with pulmonary tuberculosis with regard to sanatorium treatment.

(ii) Rules for diet are positive rather than negative, i.e., it is not generally a question of ruling out certain foods, but of insisting on generous quantities of the right food. Some exclusion rules are sensible, alcohol certainly, known gastric 'irritants' (at least during the early stages of treatment) and bulky or 'indigestible' foods, such as new rolls and bread, stodgy suet or milk puddings. The essential foods are animal fats, first-class protein, the vitamins and iron—milk, butter, cheese, meat, fish, eggs, fruit juice, cod-liver oil, or a concentrate, and so long as the hæmoglobin level is less than 90 per cent, 90 grains daily of iron and ammonium citrate. If economic circumstances have been particularly bad, it is probably wise to 'saturate' the patient also with vitamins B<sub>1</sub> and C by giving the equivalent of 5,000 units of vitamin B<sub>1</sub> and 200 mg. of ascorbic acid daily for a fortnight.

(iii) As with most other illnesses, if the patient can have his bed out of doors so much the better; the benefit is probably psychological, but is definite.

(iv) No purgatives should be used. A paraffin-magnesia emulsion, with occasional enema if necessary, should be used.

(v) Tobacco need not be abandoned, but should not be abused.

(vi) *Dental treatment.*—This will depend rather on one's personal bias for or against the 'focal sepsis' theory. Wholesale extractions are certainly a mistake, whatever the state of the mouth, and especially in the early stages of treatment, when a debilitated patient may easily react by developing a septicæmia against which he has no immunity. For my own part, I regard dental caries and pyorrhœa as one symptom of diet deficiency not necessarily curable by diet, since some of the damage is irreparable, but of little consequence *per se*. An edentulous patient should of course be provided with dentures if he is to take a reasonable diet.

The progress of the patient must be judged either by x-rays or gastroscopy, or both. It may be necessary, but it is always unwise to do without. If the ulcer is a chronic one and the patient symptomless, an x-ray can be taken after two months of treatment; it will cause the patient unnecessary disturbance to do it earlier, and is a waste of time for the radiologist. Recurrence of symptoms under treatment almost certainly means a wrong diagnosis. If the radiologist

cannot report substantial change towards healing after a few weeks in a relatively acute case, or two months in a chronic one, carcinoma should be suspected and resection considered. Benzidine reactions should be done for occult blood in the stools every week or ten days (a bedside test, no more difficult than testing for acetone in the urine). Positive reactions persisting after three weeks of treatment should raise serious doubt about the diagnosis, provided hæmorrhoids have been excluded (if these are present they should be promptly treated).

(B) *The patient has had an evident gross hæmorrhage (hæmatemesis or melæna).*

It is very necessary that one should be cautious about the diagnosis, and prognosis must be guarded. There are many causes of severe hæmorrhage from the stomach—e.g., cirrhosis of the liver, whether alcoholic or part of a hepato-lial fibrosis (Banti's disease), and carcinoma (uncommon as a cause of profuse hæmorrhage). I have recently seen a case of acute leukosis (leukæmia) in which hæmatemesis was the first symptom calling for medical attendance.

(i) *A patient with hæmatemesis of more than half a pint should be at once transferred to hospital or nursing home, since his life may depend upon blood transfusion.* There is no longer a controversy on this point: the theoretical danger of moving him by ambulance is infinitely less than the risk of repeated bleeding (or steadily continuing bleeding) carrying him, possibly within a few hours, beyond help. It is impossible to predict that a patient with a first hæmorrhage will fall into the group of 'mild' cases with probably a 100 per cent recovery rate; the 'severe' cases not treated by transfusion have a mortality rate of about 30 per cent. Authorities differ as to the exact indication for transfusion, some taking a hæmoglobin level of 50 per cent, others 40 per cent, or even 30 per cent as the critical point; the higher figure is probably the best since transfusion for hæmorrhage not accompanied by serious disease of blood or blood vessels has no dangers, and the recovery of the patient is always hastened. Drip transfusion (of several pints of blood if necessary) is increasingly used as being more effective, and as providing a controlled rate of replacing lost blood. A single transfusion of 20 oz. of blood-citrate mixture will not raise the hæmoglobin level more than 10 per cent, but may be all that is necessary to save life if hæmorrhage has actually ceased. Apart from estimations of blood volume the hæmoglobin level is the only criterion of this, and one has to remember that if it is estimated immediately after hæmorrhage a figure will be obtained which has no relation to the total blood lost (i.e., is deceptively high) since several hours must elapse before tissue fluids have restored the blood volume and diluted the existing hæmoglobin.

Transfusion without compatibility tests performed by someone experienced in their use is only justifiable in extreme emergency (i.e., in a moribund patient): a near blood relative is then the least dangerous donor.

(ii) The second big change in the treatment of hæmatemesis in recent years, and one now fully accepted as not only reducing mortality and hastening convalescence, but also as making treatment much more tolerable for the patient, is liberal feeding. It is odd that the traditional starvation treatment should have remained the standard for so long, yet it required great courage and determination on the part of Meulengracht who introduced this revolution three years ago, to begin his trials. His total mortality among 250 cases of hæmatemesis was less than 1 per cent; of a similar group treated in a neighbouring hospital in Copenhagen, on exactly the same lines except for the diet, 8 per cent died, and this was also Meulengracht's death rate previously.

The simple theory behind his treatment is that a full stomach is less motile, has less unneutralized acid, and supplies to the patient foodstuffs and minerals which he urgently needs in blood regeneration.



Practice has completely confirmed his theory in numerous clinics. Feeding abolishes rapidly the intense thirst and discomfort, and hastens by weeks the return to a normal hæmoglobin level.

The diet need follow no absolute rule. Meals may be taken at ordinary times, and the food be of the kind mentioned above (the preparation at first should be by steaming, meat should be minced or mashed and vegetable sieved; helpings should be of moderate bulk). Feeding should begin immediately after the patient has stopped vomiting. Fluids can be given according to desire (broths, soups and alcohol alone excepted). Vitamin additions are advisable from the first, and iron in full doses should always be given. No attempt should be made to relieve constipation for several days.

(iii) Morphia, the old standby in treatment, is useful, particularly if the patient is frightened, but gr. 1/6 by injection, repeated two or three times during the first day or two is all that is necessary. Saline rectal infusions are rarely required if feeding is being employed (with transfusions if necessary).

(iv) Operation as an immediate treatment in hæmatemesis has been seriously practised, but has almost no support in Great Britain. So long as one patient in three with severe hæmorrhage died, there were good grounds for experimenting with surgery, although it was never possible to predict that the patient who had lost 20 or 30 ounces of blood would not recover spontaneously, and the possibility of ligating the bleeding vessel was always problematic. When transfusion and early feeding can reduce total mortality from hæmatemesis to one in a hundred, surgery remains the last remedy, i.e., the surgeon operates when bleeding continues unabated after some days, drip transfusions maintaining the blood volume before and during the operation.

The patient who has been treated on these lines and who has shown no signs of recurrent hæmorrhage after 10 to 14 days can be safely and advantageously

transferred to his own home to continue convalescence, provided that the source of his hæmorrhage is subsequently to be fully investigated.

(C) *The treatment of gastric ulcer cases not included under headings A and B is by operative surgery, the indications for which are:—*

(a) Perforation (suture).

(b) Long continued profuse hæmorrhage (ligature or resection).

(c) Chronic ulcer not improving after two or three months of 'medical' treatment (resection).

(d) Fear of carcinomatous change (resection).

(e) Pyloric stenosis or hour-glass contracture giving rise to severe symptoms (short circuit or resection).

Perforations apart, the actual decision to employ surgery is not an easy one, and ought to be regarded with great gravity. In hospital practice there should be bedside discussion of the case between physician and surgeon (and radiologist if possible), but it is best that the surgeon's opinion should be sought early in the course of treatment, at the time when the possibility of operation becoming necessary first arises. There is no evidence that short circuit operations hasten recovery when obstruction is not present, and it is always worth while to postpone operation even for pyloric stenosis, until repeated x-ray examination makes it certain that gross delay in emptying cannot be remedied by a month of rest, good diet and gastric lavage; this delay, of course, is only justifiable provided the appearances do not suggest neoplasm.

The general practitioner's function in the treatment of gastric ulcer is that of preliminary diagnosis, insistence on investigation, encouragement during tedious treatment, and the responsibility of seeing that every possible opportunity is taken for the best treatment. His function cannot be reckoned as either greater or less than that of the specialist's, and unless circumstances force him to do so, it is a profound mistake for him to attempt to combine the two in his own person.

## Reviews

### AN ATLAS OF THE COMMONER SKIN DISEASES.—

By Henry C. G. Semon, M.A., D.M. (Oxon.), F.R.C.P. (Lond.). Second Edition. 1940. John Wright and Sons Limited, Bristol. Pp. xii plus 272, with 120 plates produced by direct colour photography from the living subject. Price, £2 2s.

This atlas contains 105 colour plates of what the author classes as common skin diseases and 15 of less common ones, a total of 120.

The plates are extraordinarily well produced and with very few exceptions the colours are true to nature. No attempt at classification is made, the plates being arranged in alphabetical order of the diseases they portray, and in the reviewer's opinion this is by far the better arrangement because skin diseases as a whole do not admit of division into clearly defined groups except in a very restricted sense.

The short descriptions of the plates and outlines of diagnosis and treatment are clear, concise and informative, and a pleasing feature is that in many instances there are references to the course and diagnosis (or wrong diagnosis at first) of the actual case from which a plate is taken so that one lays the book down with the feeling that he has been attending a skin clinic where specially selected cases have been skilfully demonstrated by an expert.

If one may offer a mild criticism it is that plate XLVII of Bockhart's impetigo is a depiction of the advanced and rather chronic condition into which it subsequently develops and would not be helpful in diagnosis of an early case. Unfortunately the book will not be of great use in India or other countries where the majority of persons have dark skins, because

the appearances, particularly of the erythematous and pigmentary skin conditions, are very different from their appearance on white skins. A similar atlas of dark-skinned people is badly needed.

The price £2 2s. is not high considering the excellence of the contents of the book, but it is a lot of money for a general practitioner to spend on a book that deals with only a small section of the cases he is likely to encounter in his daily round.

P. A. M.

**ASTHMA AND THE GENERAL PRACTITIONER.—**By James Adam, M.A., M.D., F.R.F.P.S.G. Baillière, Tindall and Cox, London. 1939. Pp. ix plus 157. Price, 6s.

THERE has been a growing tendency to consider all cases of bronchial asthma as allergic in origin, so much so that patients suffering the symptom-complex of asthma, but showing no signs of allergy, are often labelled as cases of asthmatoïd bronchitis and not of asthma. This classification of cases into asthma and asthmatoïd bronchitis is not very much appreciated by workers in countries like India where allergy does not seem to play a very important rôle in bringing about the syndrome. A simpler and more acceptable terminology would perhaps have been to use the term asthma for all the cases suffering from the syndrome and then to divide the cases into 'allergic' and 'non-allergic' according to whether or not 'allergy' was responsible. From this point of view the publication under review is a pleasant departure from the present-day 'allergy'-ridden literature on asthma. The author recognizes that asthma may or may not be of allergic

origin, and states that 'asthmatics are about half-and-half allergic and non-allergic'.

Dr. Adam believes that there exists a 'toxic factor' in all cases of bronchial asthma and that the proper recognition of this fact is most important from the point of view of the treatment of the condition. It is considered that allergy tends to grow on a 'toxic soil' and therefore detoxication of the patient plays an important part, even in the treatment of allergic cases. It is only in a minority of cases that a special allergen may be more important for successful treatment. This 'toxiosis' is supposed to be brought about by a 'sluggish liver' and 'sluggish adrenal function'. According to the author, the most satisfactory evidence of the presence of the toxic state lies in the results of treatment along detoxicating lines, whereby the sallow complexion of the chronic asthmatic clears side by side with the improvement of the asthma. The observations of the different workers regarding the biochemical changes in asthma would, no doubt, tend to support the presence of a basic toxic factor in all cases of asthma.

The general treatment consists 'largely in changing the patient's habits as to food, clothing, exercise and environment—in short, it is a problem in hygiene'. 'The aim of this treatment is three-fold: (1) to rid the patient of toxic material, protein or other, (2) to help enzyme action, intracellular or secretory, (3) to tone up the involuntary nervous system with its partners, the adrenals and the skin'. Digestion should be improved, it may be necessary to give acid-pepsin mixture. A daily movement of the bowel is essential, in addition a weekly mercurial, followed by saline should be given regularly for one or two years. At the outset, it may be necessary to lavage the colon once or twice a week. The food should contain adequate supply of calcium and the different vitamins, in this connection food may have to be supplemented by special preparations of calcium and vitamins. Sugar, especially in the form of sweets, should not be taken in excess. The patient should be encouraged to take open air exercises and lead an active life.

The book will certainly help the general practitioner in tackling the difficult problem of treating the chronic, intractable cases of bronchial asthma.

D.

**ROENTGEN TECHNIQUE.**—By Clyde McNeill, M.D. 1939. Baillière, Tindall and Cox, London. Pp. ix plus 315, with 268 illustrations. Price, 27s. 6d.

The present volume deals mainly with roentgen anatomy and positioning of the patient.

In many instances line drawings of remarkable clarity have been substituted for half-tone reproductions of skiagrams—a scheme which has much to recommend it.

The reader's convenience is further catered for in the arrangement of the descriptive matter and illustrations. The two pages facing the reader usually contain a complete description of one position—illustrations on the left, descriptive matter on the right. Furthermore, on the left hand page, below the photograph of the patient and apparatus in position, is either a line drawing or half-tone print of the normal appearances.

The standard positions are described so that the whole procedure can be carried out with simple apparatus, and therefore the book should be of particular interest to those who have to work with the cheaper types of apparatus, either in small hospitals or private consulting rooms.

The style is concise and clear. Most of the procedures are described in as few words as possible; but references have been added in some cases for the benefit of those who wish to see the original papers.

Owing to its small compass the work is necessarily incomplete; but, it is amazing how much correct and valuable information the author has condensed in a small volume.

J. A. S.

**MARIHUANA: AMERICA'S NEW DRUG PROBLEM. A SOCIOLOGIC QUESTION WITH ITS BASIC EXPLANATION DEPENDENT ON BIOLOGIC AND MEDICAL PRINCIPLES.**—By Professor Robert P. Walton. 1938. J. B. Lippincott Company, Philadelphia and London. Pp. ix plus 223. Illustrated. Price, 12s. 6d.

*Cannabis sativa* or Indian hemp grows spontaneously in almost all climates and places and is easily available. It is perhaps the oldest narcotic which has been indulged in by the human race and its use in one form or another prevails all over the world. The drug is habitually used to a considerable extent in India, Egypt, North Africa, and Central Asia, and millions of people are addicted to it. In his admirable monograph Professor Walton has made an attempt to make a survey of our present knowledge of 'hashish' or 'marihuana' as it is called in America. Its use during the last ten years has become a serious menace to the population of some of the states in the United States of America and Mexico and has been a source of great anxiety to the Bureau of Narcotics. The drug is smoked in form of cigarettes popularly known as 'reefers', 'muggles', 'Indian hay', 'tea' and 'goof butts'.

The marihuana or *Cannabis indica* problem is not connected with any one section or community or country. It appears to be a universal evil affecting the young and the old, the rich and the poor, rural and urban areas. Even the school children are taking to its use. Of particular value to the professional reader are the chapters devoted to acute and chronic effects of hashish, in which the author has analysed the recorded descriptions of its effects and has carefully classified them. The drug affects the entire nervous system, especially the higher nervous centres. Illusions, inordinate and senseless laughter, loss of idea of time and space are among the first effects observable. The intense intoxication may lead to uncontrollable irritability, which may lead to crime. Amnesia often occurs and there may even be transient mania; permanent insanity is also said to occur. Save in extreme cases, deprivation of the drug appears to cause no serious abstinence symptoms in marihuana addicts, and the tendency to chronic addiction is much less than that observed with the drugs such as morphine, heroin, cocaine, etc. These facts, together with the relatively low degree of physical deterioration associated with the use of hemp drugs, in moderation, have, of course, been known for a considerable time. Professor Walton, however, rightly stresses that the most serious aspect of the problem in America is the extent to which the vice promotes juvenile delinquency, serves as an introduction to more dangerous drugs, and increases the use of extreme violence by criminals.

Any attempt to eliminate the marihuana habit must be based on accurate scientific knowledge of the drug, its origin, growth, and the various forms in which it is taken, and its physiological and harmful effects. So far there has been no such scientific work on the subject except perhaps the recent work of Chopra and Chopra in India (*I. J. M. R.*, Memoir No. 31, July 1939). Professor Walton's book will be equally of interest to the layman and the professional readers, and deserves wide publicity.

R. N. C.

**THE LOUSE: AN ACCOUNT OF THE LICE WHICH INFEST MAN, THEIR MEDICAL IMPORTANCE AND CONTROL.**—By Patrick A. Buxton, M.A., M.R.C.S., L.R.C.P., D.T.M. & H. 1939. Edward Arnold and Company, London. Pp. ix plus 115. Illustrated. Price, 7s. 6d.

Wars have a way of changing values and altering emphases, of both individuals and things, of ship-builders and of iron ore, and, whether we consider the louse as an individual or a *thing*, the war certainly has, as one of its minor results, underlined this arthropod. The louse, a social stigma in some communities, evidence of virility in others, is to the soldier in the trenches and to the refugee seeking shelter in



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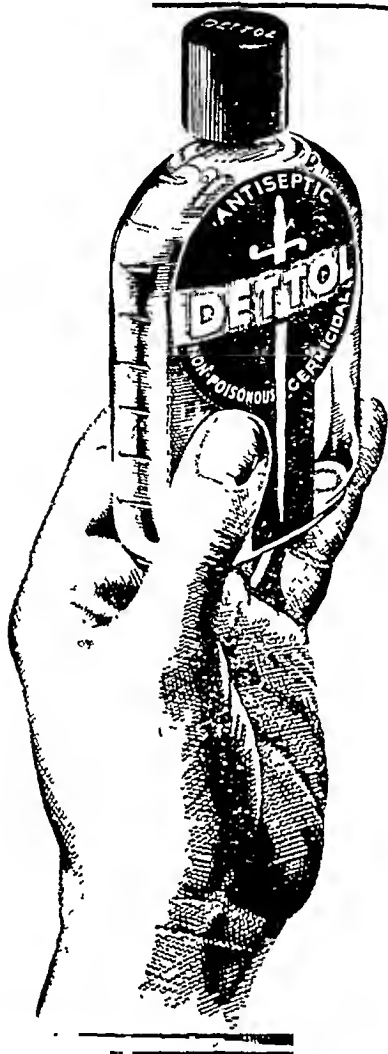
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a foreign country just an unpleasant fact and a subject of daily struggle. Professor Buxton's book is therefore not only welcome but very opportune. It was not, however, a hurried production rushed into print to catch a popular demand, but a well-considered treatise which would have formed, and we hope still will form a chapter in a more comprehensive work on medical entomology. Professor Buxton, possibly because his interest was stimulated during the Mesopotamian campaign in the last war, has always paid special attention to the louse and, in fact, if the reviewer may generalize from his own association with the writer, is seldom without one of these arthropods on his person, not of course at large, but confined in one or other of his ingenious devices shown on pages 99 to 101 of this excellent book.

Anyone interested in the louse from a personal, from a sanitarian's or from a medical point of view will find this book invaluable. The chapter on the entomology of typhus and trench fever is one of the clearest expositions on the aetiology of these diseases that the reviewer has had the pleasure of reading, and for this reason he can strongly recommend the book to anyone interested in either typhus or lice-borne relapsing fever (though he cannot subscribe fully to the author's statement that epidemic typhus fever never occurs in India, or on the other hand that lice are common, generally, in India—the Bengali doctor often sees his first louse while he is taking his post-graduate course in Europe). For entomologists, it is of course essential that they should acquire a copy of this excellent book.

**CONSERVANCY FOR TEA ESTATE LABOURERS IN INDIA: A DISCUSSION ON METHODS OF MEETING SOME OF THE DIFFICULTIES ENCOUNTERED IN INTRODUCING THE BORED-HOLE TYPE OF LATRINE.**—By B. A. Lamprell, M.R.C.S., L.R.C.P., and G. C. Ramsay, C.I.E., O.B.E., M.D., Ch.B., D.T.M. & H. (From the Ross Institute of Tropical Hygiene, London School of Hygiene and Tropical Medicine.) Published by Ross Institute Industrial Advisory Committee. Pp. 31. Illustrated

This brochure is a good practical account of how bored-hole latrines should be constructed. It also describes the main objections and difficulties of construction of this type of latrine on tea estates in India, and how they may be overcome.

Written as it is by a practising tea garden medical officer and an ex-tea garden doctor who is still closely associated with the health problems of the industry, it should carry more weight than one written by an outsider, who could be criticized as not knowing the difficulties and objections from personal experience.

It is supported by statements of three progressive tea estate managers who advocate this system of conservancy. This should do much to combat the opposition to these latrines that still unfortunately exists in certain districts.

The brochure contains a full description, including costs and drawings, of how bored-hole latrines should be constructed and if these are closely followed, and not modified out of all recognition as such instructions frequently are by individual managers, it should do much to overcome the opposition to their introduction. It should be, and no doubt it is, in the hands of all tea estate managers.

P. A. M.

**BIBLIOGRAPHY OF NUTRITION IN INDIA.**—By N. Gangulee, C.I.E., Ph.D. 1940. Oxford University Press, London, Humphrey Milford. Pp. viii plus 79. Price, Rs. 3. Obtainable from Oxford University Press, Bombay and Calcutta

This is a bibliography that both the physician and the research worker will find very valuable. Work on nutrition has only been taken up seriously in India during the last few years, but the references already make a formidable array.

Dr. Gangulee has done a valuable service to workers in India by compiling this useful bibliography. It is a book that should be in every medical library in this country.

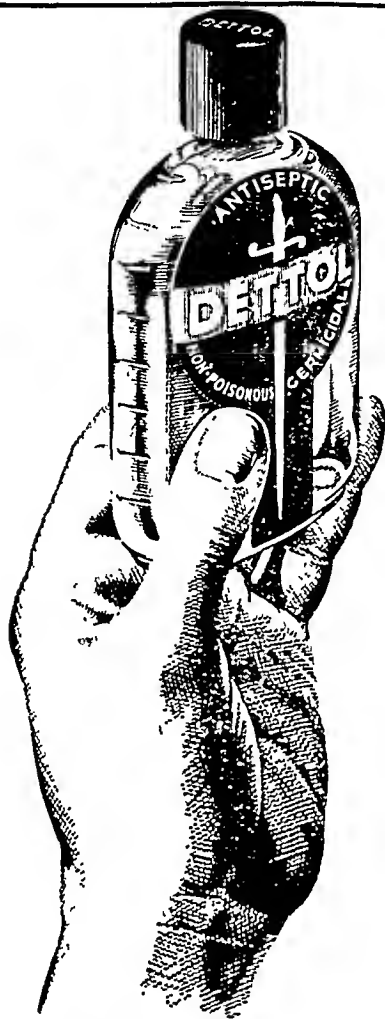
**MEDICAL RESEARCH COUNCIL. SPECIAL REPORT SERIES, NO. 237. 'BREATHING MACHINES' AND THEIR USE IN TREATMENT: REPORT OF THE RESPIRATORS (POLIOMYELITIS) COMMITTEE.** Published by His Majesty's Stationery Office, London. 1939. Pp. 90. Illustrated. Price, 2s.

The preface of this report not only gives an excellent idea of the scope of the book but summarizes the findings in a way that, we think, will interest our readers. We have therefore reproduced it *in extenso*.

'This report summarizes the present state of development of mechanical apparatus for preventing asphyxia due to respiratory paralysis. Under their more striking but less accurate description as "iron lungs", these machines have become a subject of widespread interest in recent years, because of certain reported cases in which they have maintained the lives of individuals who otherwise would have been expected to die at once. Before the subject received the increased newspaper publicity which followed the generous offer by Lord Nuffield to manufacture the Both type of machine and supply it free of charge to hospitals throughout the Empire, the Council had already appointed a Committee to examine the various forms of machine available and to consider the problem from the physiological point of view, as well as with regard to questions of cost and distribution. The immediate stimulus to this action was a request to the Council from the Ministry of Health for guidance regarding the supply of these machines, and as to their respective merits for the treatment of cases of respiratory paralysis, particularly in acute anterior poliomyelitis. The epidemic of poliomyelitis in England and Wales in 1938, although small in comparison with some of those which have occurred in other countries, was nevertheless attended by a number of cases of respiratory paralysis sufficient to demand serious attention from this point of view'.

'Artificial respiration is, of course, needed in many other conditions than poliomyelitis. Asphyxia is usually an acute emergency, so sudden that every adult should be able to carry out artificial respiration by hand, and so brief that the manual method is generally all that is required. Its commonest causes are carbon monoxide poisoning and drowning, and for these immediate treatment by the manual method is essential. There are, however, instances—such as certain cases of poliomyelitis and diphtheria—in which spontaneous breathing remains in abeyance for so long that artificial respiration by hand becomes not only tedious but wholly impracticable, and for these some form of breathing machine is necessary'.

'When the Committee started work the problem to be studied appeared relatively easy, for most medical men were familiar only with two types of breathing machine—the Drinker apparatus or "iron lung", and the Bragg-Paul "pulsator". These represented two different principles of artificially maintaining the action of the lungs, which might be briefly described as negative and positive pressure methods. Further consideration, however, revealed that the problem was one of great complexity. Instead of two, there were many types of apparatus to be considered; and the best type of machine for one condition was not necessarily the best for another condition. Again, cost had to be considered, and also the degree of skill and amount of attention required for efficient working of any machine. On such points as these, moreover, rested the decision as to the best means of maintaining a service that would work effectively throughout the country. All these questions and many others are considered by the Committee in the following pages. They describe the great majority of the machines available; they discuss the advantages and disadvantages



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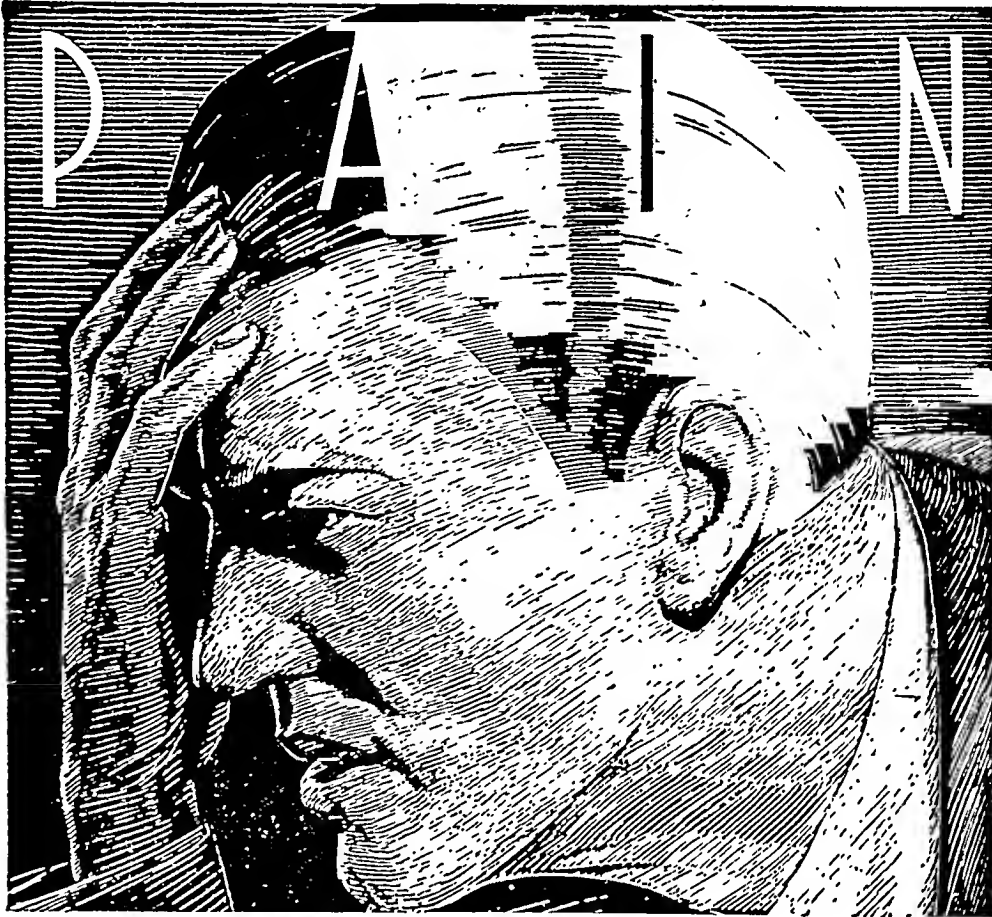
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Two hundred and forty-nine deaths were recorded during 1938, as having occurred from relapsing fever, 8,709 from enteric fever and 155 from kala-azar. The corresponding figures from these diseases for 1937 were 227, 9,366 and 181, respectively.

The number of deaths reported from influenza during the year under report was 528—249 from urban areas and 279 from rural areas.

During 1938, dysentery and diarrhoea were responsible for 21,015 deaths representing a death rate of 0.13. The corresponding figures for the preceding year were 17,126 and 0.35, respectively, and the mean ratio for the previous five years 0.34.

#### *Respiratory diseases*

These diseases were responsible for 46,957 deaths as compared with 44,628 in the preceding year. The death rates for the two years and the mean for the previous five years were 0.07, 0.92 and 0.89, respectively.

The incidence of cerebro-spinal meningitis was again low this year. The total number of deaths reported from this disease was 84 against 158 in the preceding year. Of these 74 deaths were reported from towns and 10 from rural areas.

Epidemic dropsy was responsible for 90 deaths compared with 64 in the preceding year. Of these, 65 were reported in urban areas and 25 in rural areas.

During the year 1938 a large number of bored-hole latrines were constructed in villages, and there is a demand from the better class rural population for such latrines to serve as domestic privies. In the Fyzabad district alone, 46 such latrines were constructed in the year.

The medical officer in charge of the Partabgarh Health Unit, as the result of field experiments carried out in the health unit area, drew up plans and specifications for a 'bored-hole' type of absorption pit to receive house sullage. These have been circulated and in places where they have been put up, have been found to be far superior to the soakage pits that used to be constructed before. Such pits are particularly suited for village schools, market places and fairs. When provided with foot-rests they can serve as urinals. These pits require less space, are more economical and do not need much care for maintenance. They are thus a great improvement over the cesspools which are a source of great nuisance in villages, and need the daily services of sweepers to look after them to prevent them from overflowing.

Eight new maternity centres were opened during the year under report. Total number of centres is now 301 (147 rural and 154 urban).

There is no Red Cross maternity hospital in the United Provinces. Clinics were held at maternity and child-welfare centres. The staff paid ante-natal and post-natal visits, trained indigenous *dais* and organized baby shows, magic lantern demonstrations and lectures during exhibitions, fairs, etc.

The total number of cases conducted by the staff with or without *dais* was 47,950 while that of cases not attended to by Red Cross workers in the same area was 111,294. The Director of Maternity and Child-welfare inspected the maternity and child-welfare work both in rural and urban areas of 18 districts. During the course of these inspections she also saw expectant mothers and babies in their homes and afforded the necessary advice to workers and the public.

The training of probationer assistant midwives in domiciliary midwifery and house-visiting was, as usual, undertaken at the Provincial Training Centre, Lucknow, and was supplemented by three months' hospital training at the Dufferin Hospital and one weekly lecture and demonstration at the Queen Mary's Hospital. Twenty-six probationers were declared successful during March and September examinations and were awarded the certificate by the State Medical Faculty.

Facilities for midwifery training also existed in the Cawnpore maternity and child-welfare centre. The Dufferin and mission hospitals also trained these workers for their own needs.

A serious effort continued to be made to train *dais* especially in the 25 maternity and child-welfare centres where medical women or health visitors were employed and also in the Health Unit, Partabgarh. A few *dais* were trained in connection with the rural development schemes.

It has been calculated roughly that of all the school boys examined, about 20.9 per cent have one defect only, 14.5 per cent have two defects and 10.1 per cent have more than two in the urban areas as compared to 34 per cent, 13 per cent and 7.5 per cent, respectively, in the previous year.

It will thus be seen that there were not less than 55.5 per cent defectives to share all the defects as compared with 54.5 per cent in the previous year in the urban areas.

*Poor nutrition.*—In the larger urban areas this defect was found to be 19.4 per cent as compared to 12 per cent in the last year.

Of the five bigger towns, Cawnpore has recorded the highest figure of 22.5 per cent and Lucknow the lowest 10.7 per cent. In the eight smaller municipalities there is a great variation in the observations, Meerut recording the minimum percentage of 9.43 and Bareilly the maximum of 43. In the rural areas this percentage was 18.1 as compared to 18.3 in the last year. Such a wide variation is chiefly due to personal factors of the officers concerned and lack of definite standards and means of judging the condition.

Poor nutrition is not so much due to poverty as to lack of knowledge about balanced diet. The school health officers give suitable advice on this subject both at the clinics and in the schools while delivering lectures.

#### THE NINTH ANNUAL REPORT OF THE ASSOCIATION FOR THE PREVENTION OF BLINDNESS, BENGAL, 1938-39

THE Association has now completed the ninth year of its existence. It has grown into one of the chief utility services in Bengal, and has amply justified its existence by the amount and quality of the services rendered to the Province in general. It is gratifying to note that mass consciousness is gradually awakening to the problem of prevention of blindness, and the diagnosis and the cure of eye diseases.

The committee has been inundated with appeals for assistance at the different centres of its activity; but it is much regretted that many had to be turned down, owing to the still limited resources at their command. Enquiries for help and advice continue to pour in from other provinces, especially with regard to the equipment and the establishment of travelling dispensaries, in the starting of which work it is our proud privilege to be pioneers in the field of India. The idea was adopted from Egypt but the dispensaries were equipped in a far less ambitious way than in that country owing to insufficient funds.

During the year under review, an innovation has been made in the activities of the Association, namely, the eye examination of children in schools and orphanages of Bengal. This has been neglected in the past, and is now being gratuitously done by one of the trained honorary workers.

The work done by the two travelling eye dispensaries of the Association, namely, the Jubilee Travelling Eye Dispensary and the Travelling Eye Dispensary No. II, has been enormous. Each unit has two medical officers who carry out propaganda work in the prevention of blindness and care of the eyes, by lectures, magic lantern demonstrations, cinemas, posters and pamphlets, etc. Systematic eye examination of school children was arranged and sample surveys of blindness in the villages were undertaken. Lectures in schools and public places were given and, in addition, they carried out routine curative work in subdivisional hospitals, and, where available, in private hospitals. Operative work was undertaken at most centres the dispensaries visited, and where indoor accommodation was available. All operative work is suspended one

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responsible medical officers beyond argument that the control of malaria is not only possible but is an important economic factor in reducing the costs of running an estate.

The India Branch of the Ross Institute to-day consists of a Principal, Indian assistants and research centres, subsidized by the Ross Institute. But, in addition, a large group of medical officers and planters are working in close association with the Ross Institute; they are, in fact, if unofficially, a part of the Ross Institute's organization and an essential part. Progress started with Dr. G. C. Ramsay's original work at Labac, which indicated the lines on which malaria could be controlled economically in Assam as in Malaya. To enable his work and knowledge to become available to the whole Indian Tea Industry, the branch was founded in 1930 and the full-time services of Dr. Ramsay obtained. The Branch opened, equipped and subsidized a number of field research laboratories in different parts of Assam and Dooars, under estate medical officers, who readily gave their voluntary services to supervise the work. These centres were not only of great value to the institute and to the tea estates in the prevention of malaria, but they were also helpful to the medical officers in solving problems in connection with other diseases.

The tea industry owes much to Dr. D. Manson, Dr. G. Fraser, Major C. S. P. Hamilton and Dr. G. C. Harrison, who have been indefatigable in advancing knowledge of the control of malaria and other diseases in Northern India tea gardens. Southern India was not overlooked, and we are also indebted to Dr. J. E. Measham for organizing the first Ross Institute Field Station in Southern India. This was followed by other research centres in Southern India, and we have had the valuable assistance of Dr. P. K. Govindan Nair. There are many other doctors in Assam whose co-operation and help have been of great value, especially Dr. F. C. McCombie, Dr. B. A. Lamprell, Dr. G. G. Terrell, Dr. G. Macdonald, Dr. H. C. Berlie and Dr. W. N. Stirling.

In the chief field stations it was possible to train a staff of Indians as malaria surveyors and laboratory assistants who would be absorbed by the estates to assist in the control of malaria. The number of Indians trained in this work by Drs. Manson, Fraser and Measham and others now exceeds 400. The majority of these are employed by the tea industry and are on the pay-roll of estates. Industries outside tea also employ Indians trained at the Ross Institute centres.

The co-operation of the individual planter is of primary importance. Unless the planter himself is interested in the control of a disease and realizes that it is just as necessary for him to have a healthy labour force as it is to have healthy tea bushes, malaria control work cannot succeed. To deal with this side of the work an annual Malaria Control Course for laymen was started at the Ross Institute in 1929, when about a dozen attended. It is estimated that over 1,000 persons have attended the course since it began, and that 590 of these were planters. This year, as is detailed later in this report, the attendance was 222, of whom 120 were tea planters from India. The course is free.

During the past eight years Dr. G. C. Ramsay has visited practically every tea estate in India, many several times, and the demand for his services has been so constant that the time he has been able to spend on individual gardens, by force of circumstances, has been limited. Subscribers have also asked him to help in other directions, which has resulted in useful work being done in certain sugar districts, in jute mill areas, cotton ginning factory areas, and on various mines in India.

#### *The Control of Malaria on Estates*

Dissections of thousands of mosquitoes at various research centres have confirmed Dr. Ramsay's findings at Labac that the only anopheles mosquito we have to control in the Dooars and Assam is *A. minimus*. The possibility of other carriers is not overlooked, but

so far our control is directed against the one species *A. minimus*. In Southern India *A. fluviatilis* is the principal carrier in the Anamallais and Meppadi areas. In the Peermade district two species have been incriminated, *A. fluviatilis* and *A. culicifacies*. Having found the species responsible for carrying malaria, our efforts have been directed against the breeding places of known vectors and other species are ignored. This is known as 'species sanitation' and is the most economical method of dealing with malaria in settled populations.

It was known in Malaya as far back as 1909 that certain malaria carriers could be controlled by the preservation of dense shade. In Assam it was demonstrated that *A. minimus* could be controlled by the growing of dense shade over channels and streams and in swamps. Where this can be done it is one of the cheapest methods of control. The shade plants mostly grown in Assam are *Duranta*, *Hibiscus*, *Basak*, *Lantana*, *Eupatorium*, *Tarapat* and *Bamboo*, and in Southern India, in addition to *Tarapat* and *Duranta*, leafy plants such as *Nilgiri Woods*, *Wild Camphor* and *Wild Cardamom* are being used. Other methods of control are employed according to circumstances, such as oiling, Paris green, flushing, draining, vertical draining, stone packing, oil booms, shading the edges of tanks, etc. Many experiments have been made with drugs. Prophylactic measures by drugs give only temporary results and are resorted to only in exceptional circumstances. Where the breeding places of the mosquitoes are properly controlled the use of drugs, except as treatment, is unnecessary.

Detailed information regarding the modern method of flushing streams by means of a siphon has been circulated through the Industrial Advisory Committee of the Ross Institute. The use of siphons was introduced by Dr. G. Macdonald in Ceylon, and this method is now widely used to control streams on tea gardens in Ceylon. The siphon was demonstrated at the Malaria Control Course for laymen. Siphons can be used singly or in batteries of two, three, four and five upwards, according to the size of the streams.

[The reports of the various departments and research sections are so condensed that they do not lend themselves to abstraction with any prospect of giving a comprehensive review of the many activities of the London School in the space at our disposal. We have therefore this year been compelled to confine our abstract to the remarks of the Chairman of the Finance and General Purposes Committee and the Board of Management, and to the activities of the Ross Institute in India.]

#### DIRECTOR'S REPORT ON THE WORK OF THE EASTERN BUREAU, SINGAPORE, LEAGUE OF NATIONS, HEALTH ORGANIZATION, FOR THE YEAR 1939

THE Deputy Secretary General in a broadcast address from Geneva on 21st October stated, among other things:—The League will still, despite the war, find a large field of usefulness. Public Health matters will bulk very large, perhaps even larger than before the war. The League's worldwide service of epidemiological intelligence will be more and more necessary as national services become overburdened by the new emergencies, and as new epidemics, perhaps, develop out of the war in both Europe and Asia.

Subsequently the health committee, which met in Geneva from 20th to 24th November, considered the effect of the war on the work of the health organization. It recorded the view that the permanent services must not be interrupted since their reconstruction would be exceedingly difficult. The Singapore Bureau was mentioned as one of these permanent services whose utility was universally acknowledged.

The health committee also recalled that by agreement with the permanent committee of the Office International d'Hygiène Publique, Paris, governments of eastern countries can effect notifications required under certain articles of the International Sanitary

Convention, Paris, 1926, by means of the Singapore Bureau.

Throughout the year, including the last four months when normal methods of communication have been so profoundly altered by the war in Europe, cabled information regarding outbreaks of the major infectious diseases and their progress has been regularly received from all eastern health administrations. In no important instance has there been inconvenient delay and consequently it has been possible for the bureau to prepare and transmit its weekly bulletin regularly on time. Perhaps nothing could have better illustrated how well established is the international system of epidemiological intelligence in the Far East, of which the bureau is the centre. Without the fullest co-operation of all the countries adherent to it, the service the bureau can render would be of correspondingly less value to each one. It must therefore be a source of much satisfaction to the countries, which worked for the establishment of the bureau in 1925, and have consistently supported it since that time, to find that the hostilities in both east and west have not interfered with the carrying out of its primary function, *viz.* the collection of epidemiological information from individual eastern countries and its immediate circulation to them all.

Wireless transmission is the principal medium for the circulation of the information received by and collated in the bureau.

The broadcast messages have not only been continued at the usual times throughout the year, but towards the end of it there has been a marked advance in methods, which has come about because of the disturbance to normal communications caused by the war—one example of good coming out of evil.

The opportunity is gladly taken to express our most grateful thanks to the governments and authorities directing the wireless stations who have so consistently and whole-heartedly placed their services at our disposal, and have always responded so willingly to the demands made upon them. They are playing a most important part in preventing the transfer of communicable disease from one country to another.

[*Note.*—In addition to the usual record of epidemiology of the principal diseases in the area administered by the bureau, this year's report contains summaries of recent research work. There is also an account of the special courses in malariology held annually under the auspices of the Singapore bureau. It is a report that should be in the hands of all health authorities of the countries bordering the Indian and Pacific Oceans.—EDITOR, I. M. G.]

### THE THIRD ANNUAL REPORT OF THE INDEPENDENT MEDICAL PRACTITIONERS' ASSOCIATION, TINNEVELLY, FOR 1939-40

THE year opened with 28 members on the rolls, three new members have joined the association during the year and none left during the same period.

The association held 12 clinical meetings usually on the second Saturday of every month at Dr. L. Mahadevan's Eye Clinic, Vannarpet, when one of the members of the Association delivered a lecture which was followed by discussion by members.

The average attendance at these meetings was 14. Besides the regular meetings there were two special meetings.

### ANNUAL REPORT OF THE EXECUTIVE COMMITTEE OF THE BENGAL TUBERCULOSIS ASSOCIATION, FOR THE YEAR 1939

LAST year the members of the Tuberculosis Association of Bengal met in the midst of enthusiasm aroused by Her Excellency the Marchioness of Linlithgow's appeal for the King-Emperor's Anti-Tuberculosis Fund for India. This is the first report of the newly formed Bengal Tuberculosis Association with which is amalgamated the old Tuberculosis Association of Bengal. The close of the year 1939 saw the close of the appeal to which the princes and people of India

made a most magnificent response. The total collections amounted to over 80 lacs of rupees to which Bengal's contribution of Rs. 7,87,000 was the highest. This is one of the largest funds collected in this country for the relief of human suffering, and India will ever remain grateful to H. E. the Marchioness of Linlithgow for making this great contribution towards the welfare of her people.

According to the announcement made by Her Excellency ninety-five per cent of the collections have been returned to the provinces; and Bengal has received back a sum of Rs. 7,57,801. Of this sum, Rs. 50,000 being donation from the Calcutta Corporation was earmarked for payment to the Jadavpur Tuberculosis Hospital and has been paid to it; and a like sum representing the donation from King George V Memorial Fund is set apart for expenditure on a project to commemorate the memory of His Late Majesty King George V. The balance of Rs. 6,57,801 forms the Corpus from which only the interest is available for expenditure without the sanction of the Central Committee. By the end of the year under report a sum of Rs. 6,30,199 had been invested in Rs. 6,50,000 3 per cent loan, 1963/65, and a further Rs. 10,000 was purchased at the beginning of 1940.

This is the eleventh annual report of work in the prevention of tuberculosis and it is the first report under the new association formed as a branch of the All-India Tuberculosis Association. Although we have only been able to touch the fringe of the problem, yet when we compare our activities in 1929 when we started with only Rs. 500 and were able to look after a few hundred sufferers and compare this with our activities for the year 1939 with an expenditure of about Rs. 40,000 benefiting over 12,000 patients, visiting 35,000 homes and educating over 60,000 people in the methods of prevention of the disease, we feel a justifiable satisfaction that we have made some progress and have demonstrated the fact that this association has developed sufficiently to claim a greater measure of support from both public bodies and private individuals.

The programme of work may be resolved into the following main factors:—

(1) To help in the organization of district branches of the association, and to prescribe rules for the purpose.

(2) To get into touch with the education and public health departments, local bodies, social workers, social service organizations, railways, etc., and to stimulate interest in anti-tuberculosis work.

(3) To carry out intensive educational propaganda to educate the public in regard to the tuberculosis problem and the hygiene of prevention, particularly in relation to unhealthy habits, and injurious customs, prejudices and superstitions.

(4) To survey industrial areas, educational institutions, municipal towns, etc., to obtain information regarding prevalence of tuberculosis and to advise the authorities concerned as to measures for dealing with the situation revealed.

(5) To establish relations with existing tuberculosis institutions with a view to aiding patients in obtaining beds for care and treatment.

(6) To arrange for the training of selected medical officers, medical students, nurses and home-visitors in anti-tuberculosis work, preventive and curative.

(7) To set up tuberculosis clinics or dispensaries in connection with hospitals or independently and to provide them with specially trained staff, etc., to facilitate early diagnosis and treatment.

(8) To arrange for the systematic visiting and examination of patients and contacts by employing qualified home visitors and to render assistance to patients and contacts by providing medicines, disinfectants and nourishment.

The above list is not exhaustive but it indicates the main lines of the anti-tuberculosis campaign.

[A detailed account of the work performed during the year under these various headings is given, and indicates considerable progress has been made.—EDITOR, I. M. G.]

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\**B.M.J.*, 1937, August 28. Page 412.

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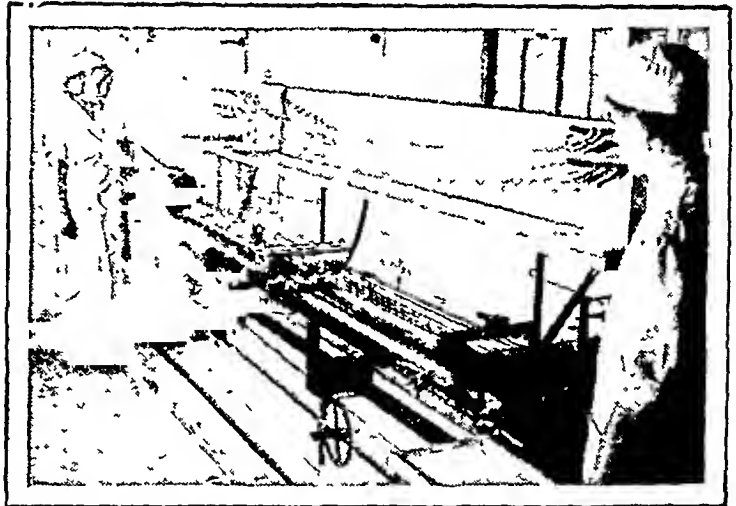
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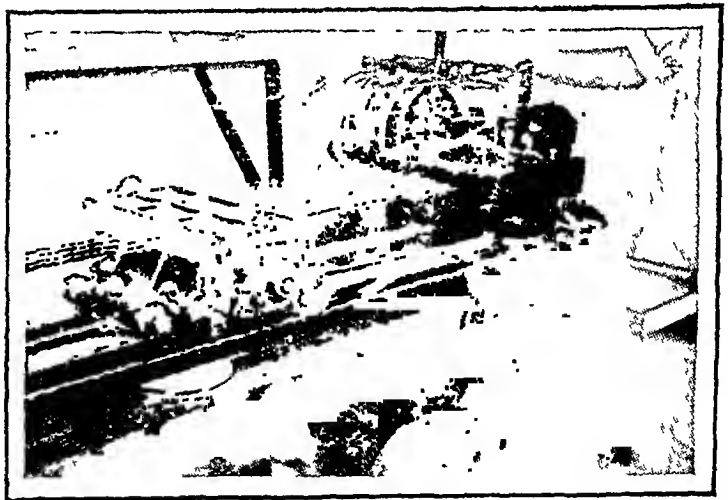
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THE TWENTY-SECOND ANNUAL REPORT OF  
THE KING EDWARD VII MEMORIAL  
PASTEUR INSTITUTE AND MEDICAL RE-  
SEARCH INSTITUTE, SHILLONG, FOR THE  
YEAR ENDING 31ST DECEMBER, 1938

*Antirabic section.*—The scheme of treatment and the preparation and dosage of vaccine remained unchanged during the year under review.

The treatment was carried out at Shillong and its authorized treatment centres which now number 24 public centres and 42 private centres. One new private centre was authorized during the year.

Two thousand two hundred and thirty-three persons applied for treatment at Shillong and its centres, the majority, of course, at the centres. Of these persons 1,875 completed treatment and among them there were 12 deaths from hydrophobia. In addition three persons applied for treatment when they were in the late incubation stages of hydrophobia and did not complete treatment because the disease supervened during the course of treatment. All three died. In our present state of knowledge nothing can be done to save such cases.

Thus among persons applying for treatment there were 15 deaths in all from hydrophobia during the year.

There were 213 'Advice Cases' who did not receive treatment or whose treatment was discontinued because they were considered to be at no risk. No less than 175 of these advice cases were among persons attending the Institute at Shillong.

Of the individuals placed under treatment and presumably at risk, 141 absconded before completing the course and there is no record of their eventual fate.

The submission of the six months' 'Health Returns' was satisfactory.

*Vaccine section.*—The following quantities of prophylactic vaccines were issued during the year:—

(1) Cholera vaccine	..	986.568½ c.c.
(2) T. A. B. vaccine	..	12.309 "
(3) Influenza vaccine	..	1,160 "

The issues of cholera vaccine were more than doubled this year owing chiefly to the cholera epidemic which occurred in Sylhet district. The re-introduction of vaccination into the bacteriophage experimental area of Habiganj resulted, however, in the supply of nearly 2 lacs of doses of cholera vaccine to this subdivision.

Cholera vaccine is prepared at this institute only from authentic and freshly tested strains of cholera vibrio, which conform with the criteria laid down by the Cholera Advisory Committee of the Indian Research Fund Association.

*Bacteriophage section.*—The total issues of bacteriophage during 1938 amounted to 495,872 ampoules of 2 c.c. each. An interesting feature is the increased supply to other Governments which was practically doubled as compared with 1937. It would appear that the value of bacteriophage as a therapeutic measure is being increasingly recognized outside Assam.

*Assam Medical Research Society*

Owing to limitation of funds, the work of the Society during this, the eighth year since its inception, has been concentrated solely on problems in connection with malaria.

The Doom Dooma Cinchona-Plasmoquin Treatment Scheme has been continued for the sixth year. In 1932-33 the spleen and parasite rates of children two to ten years were 56.5 and 40.7 per cent respectively. Following treatment these indices have been reduced to 16.06 and 12.9 per cent respectively, during the year under review. In 1936, a year of high malaria incidence, the parasite rate rose to 41.0 per cent. Many tea estates have now adopted this method of treatment as demonstrated by these experiments.

During the year 85,011 anopheline larvæ and 10,932 adults were examined. Anopheline dissections numbered 3,808 *A. minimus* being the only species found infected.

From the 1st June, 1931, the date the society started work up to the 31st December, 1938, 854,700 anopheline larvæ have been collected and their respective breeding places and dates of collection recorded. During the same period 141,201 adult anophelines have been identified and 55,586 dissected.

Experiments to determine the efficacy of cold weather and pre-monsoon anti-larval control have been continued during the year under review in the four urban and two rural areas, selected for this experiment.

The experiments have shown very encouraging results. The institution of pre-monsoon control has been followed by a significant decrease in the incidence of malaria in the six areas. This is particularly marked, by the heavy reduction in the spleen and parasite rates which has been observed among children two to ten years of age in these areas since this method of control was instituted.

In addition to the six experimental control centres, thirteen other anti-malaria control projects received financial assistance from the Government of Assam, and where a full year's survey had been completed by the society, have been supervised by the society's staff. Similarly, seven tea estates that have adopted the society's recommendations for malaria control following the completion of a full year's survey, have been visited periodically for the purpose of supervision of their control activities.

*Cholera enquiry under the Indian Research Fund Association*

On the recommendation of the Cholera Advisory Committee of the Indian Research Fund Association, a new field enquiry was undertaken during 1938. This was located in the Assam Valley.

From the findings the conclusion may be drawn that inagglutinable vibrios are natural inhabitants of waters and that such vibrios taken in with water, have little chance of survival in the gut of healthy individuals but that in those with an intestinal disturbance, they are more easily to be isolated from stools. Even if the non-fermenting type of vibrios be excluded from these figures, this does not affect the conclusions arrived at.

*The effect of bacteriophage on the agglutinable vibrio*

To determine what modifications are brought about in the cholera vibrio by the collective action of a large number of phage types, the stock 12-1 phage resistant cultures and the strain resistant to all the 12 phages kept up at the Pasteur Institute, were examined. They were derived from 653, an Ogawa strain, and have been kept phage resistant to fewer or more phage types as they were discovered, for over 5 years.

It appears from the results that all the cultures with the exception of 12-A, had undergone a definite change to rough and 12-B and 12-M had perhaps changed still further, say to the 'ro' form of Bruce White.

In order to see what effect phage has on an agglutinable vibrio when added to water, a flask containing about two litres of water, a little garden earth and a small quantity of stool was autoclaved and was inoculated with 10 c.c. of a 24-hour peptone water culture of a recently isolated cholera vibrio and 5 c.c. of therapeutic phage. In two such experiments it was found that an agglutinable vibrio of fermentation type I could be recovered for 7 and 17 days respectively, after which no growth resulted in cultures. The duration of life of the vibrio in the water was cut short by the phage, but it had not undergone any recognizable change.

Two experiments were performed, where a culture of a recent agglutinable vibrio was added to a natural collection of water after its salinity had been adjusted, cultures being made daily thereafter for recovering Ag. vibrio. Peptone water enrichment and the modified Wilson-Blair fluid medium were the cultural methods employed. In the latter case about 500 c.c. of the sample was filtered through a Seitz disc and this was washed into 40 c.c. of the medium.

In the first experiment, the water source was a shallow well 3 ft. in diameter with about 3 ft. of

water. The pH was 5.1 and salinity 0.5 parts Cl per 100,000. After adding common salt the salinity had increased to 26 parts, the pH being the same. On adding 100 c.c. of the cholera culture, the vibrio could not be recovered in 24 hours or thereafter. It will be noted that the pH was very low. A rapid diffusion of salt was also noticed. There was no natural vibrio in the water.

In the second experiment, the agglutinable vibrio was added to a tank 32 ft. x 30 ft. The pH of the water varied between 6.3 and 6.7 on different days, the organic matter (Tidy) being 0.12 parts per 100,000.

The salinity was adjusted to 70 parts per 100,000 and a litre of the culture was added to an estimated quantity of 50,000 litres of water in the tank. The agglutinable vibrio was recovered in the 24 hours' sample but not thereafter. No growth of any kind resulted in the Wilson-Blair medium throughout and in both experiments.

As this work was done during the last week of October and the middle of November, when low temperatures prevailed, it is not possible to say to what extent this factor contributed to the shortness of the period of viability of the vibrio.

## Correspondence

### EXTERNAL BURSTING OF STRANGULATED HERNIA

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—Most books on surgery describe the result of a strangulated hernia as being either death without operation, life in many cases with operation, or very rarely a faecal fistula and life, if the strangulation bursts externally. It is however given to very few of us to see any case of the latter type, hence I am sending you details of one that I saw recently.

The patient was an old man in poor health, aged about 50, a cultivator by occupation, who had had a left inguinal hernia for about four years. It had at intervals become obstructed but had always been reduced by himself without undue difficulty or delay. One month before admission the hernia had come down again, but could not be reduced, although it was very painful and he pushed it hard! He had the usual vomiting, intermittent pain, and constipation for six days, except that he sometimes passed a little flatus and stool after *deshi* purgatives which were regularly administered. It is clear, therefore, that he had an incomplete obstruction.

On the sixth day the vomiting and pain became less and on the next day he passed a normal stool, but a moderate-sized lump remained in the groin.

Throughout the illness he had been fomenting the abdomen, but after the condition improved he only applied fomentations to the lump, which six days later, that is 12 days from the onset of the obstruction, burst. The first day the discharge was mostly pus and sloughed intestinal wall, which he described as *purana kapra*, but after that a faecal fistula developed.

He was admitted to hospital with the idea that an operation would be required, but he has made an uninterrupted recovery and his wound has healed without any treatment, so that his only comment has been that he has wasted seven weeks in hospital when he could have been ploughing his field.

Yours, etc.,

E. W. HAYWARD,  
Principal Medical Officer,  
Jodhpur.

RAJPUTANA,  
26th March, 1940.

### TAKING BLOOD FOR TRANSFUSION

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—I have read with interest the article on 'Taking blood for transfusion' by Lieut.-Colonel S. D. S. Greval, I.M.S., and Dr. S. N. Chandra, in the January issue of the *Gazette*. As blood transfusion is still in its infancy in India, suggestions for making it easy to perform with safety both to donor and recipient are to be welcomed. I wish to make the following observations:—

1. Complaints regarding incisions on veins may be prevented by laying down, as the London blood transfusion service does, certain conditions.

(a) Only persons with prominent veins must be accepted as blood donors.

(b) The needle method of extraction of blood must be insisted upon and dissection of the vein forbidden.

(c) Donors must be instructed to refuse to serve if dissection is attempted.

(d) The transfusion must be performed by a skilled surgeon and not by inexperienced house surgeons.

(e) The site of the venipuncture must be infiltrated with a local anæsthetic such as 2 per cent novocain or novutox. The insertion even of a large bore needle is then painless.

2. The application of the sphygmomanometer cuff to the donor's arm has now rightly become an almost standard method of making the veins prominent. The cuff is inflated to a pressure of 67 to 70 mm. when the veins are rendered prominent without any arterial constriction. Further, the pressure is regulated more easily and with less disturbance than with an ordinary tourniquet.

3. The closed system for collection of blood is to be preferred as it is more aseptic and avoids mess. But I have not found negative pressure necessary for withdrawing blood. The authors recommend a 20 c.cm. record syringe needle to save the donor the pain caused by a large needle. The rate of blood flow through the smaller needle is necessarily slow and to improve it negative pressure is advocated. This, in my opinion, is a complication in technique. Blood transfusion is generally an emergency operation and medical men must be capable of doing it with the minimum equipment. The simplest is the best. The more complicated the apparatus the more the assistance needed.

4. The closed system described by the authors does not appear to be strictly a closed one because the 'negative pressure in the bottle is abolished by admitting air slowly through the knotted tube (hissing sound is avoided)'. That is, unfiltered air is slowly let in. It is highly desirable to filter the air admitted into the bottle and this can be easily achieved by the inclusion at intervals on the rubber tube leading to the exhaust pump of three glass filters stuffed with cotton-wool. Mere knotting of the rubber tube may prevent too rapid an inrush of air, but it is doubtful if it can be depended upon to prevent contamination of the contents of the bottle either at the time of creation or of abolition of the negative pressure.

5. I have used sodium citrate solution in a final concentration of 0.25 per cent with blood but found that fine clots tended to form and these had to be filtered out. Sodium citrate solution in a 0.35 per cent final strength is now universally used and it is also recommended by the Medical Research Council. The transfusion of blood with this slightly higher citrate content is not attended with any more reactions.

Yours, etc.,

K. S. RANGANATHAN,

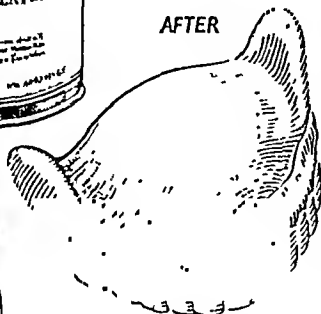
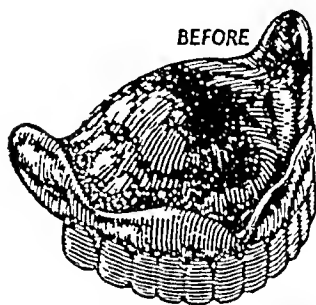
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GUINDY, MADRAS,  
19th March, 1940.



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## OBSERVATIONS ON THE USE OF NICOTINIC ACID IN THE TREATMENT OF PELLAGRA AND ALLIED CONDITIONS

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—Captain J. W. D. Goodall, in his article 'Observations on the use of nicotinic acid in the treatment of pellagra and allied conditions', which appeared in your March number, makes the statement that 'pellagra is quite common in Bengal'. He does not, however, offer any figures in support of this conclusion, and in his article he describes only three not very typical cases.

In my experience, classical pellagra, characterized by symmetrical dermatitis, lesions of the alimentary tract and mental changes, is a rare and relatively unimportant disease in India. I have visited many medical wards in search of cases and made enquiries from physicians in most parts of the country. Except for some mild cases in Vizagapatam and one or two more serious cases in maize-eating districts in the north of the Punjab, I have never observed classical pellagra, while the physicians consulted have nearly all declared that the disease is unknown. Pellagra is not a difficult condition to recognize. Some years ago I had the opportunity of studying pellagra in a maize-eating district in Roumania. In some villages in the district about 5 per cent of the population developed pellagra every spring. The hospitals and mental asylums were full of serious cases and there was a high mortality. In this case the adjective 'common' might legitimately be used. In India, on the other

hand, pellagra never assumes epidemic proportions and is not a serious public health problem.

While it has been clearly shown that nicotinic acid is effective in the treatment of pellagra, the question of aetiology has not yet been fully cleared up. One fact which requires explanation is the frequency of pellagra in maize-eaters and its rarity in rice-eaters. We have recently shown\* that the nicotinic-acid intake of poor rice-eaters may actually be below that of poor maize-eaters so that the aetiology and distribution of pellagra cannot be satisfactorily explained in terms of nicotinic-acid deficiency.

Statements that pellagra is 'common' among rice-eaters tend to confuse the issue. On the other hand, any reasonably accurate data about the incidence of pellagra in India is of value. Hospital statistics are notoriously fallacious, but percentage admission rates to hospitals drawing patients from an unselected sample of the general population may provide some information about the incidence of any particular disease.

Yours, etc.,

W. R. AYKROYD,

Director,

Nutrition Research Laboratories,  
I. R. F. A.

COONOR,

6th April, 1940.

\* Aykroyd, W. R., and Swaminathan, M. (1940). *Indian Journ. Med. Res.*, 27, p. 667.

## Service Notes

## APPOINTMENTS AND TRANSFERS

COLONEL A. C. MUNRO, V.H.S., is appointed Honorary Physician to The King, 22nd October, 1939, *vice* Colonel D. C. V. FitzGerald, M.C., retired.

The services of Colonel D. H. Rai, M.C., V.H.S., are replaced at the disposal of the Government of the Central Provinces and Berar, with effect from the 11th March, 1940 (forenoon).

Lieutenant-Colonel M. P. Atkinson, an Agency Surgeon, is appointed as an Additional Medical Officer, Indore, with effect from the afternoon of the 10th February, 1940.

Lieutenant-Colonel M. M. Cruickshank, Superintendent, Government General Hospital, Professor of Surgery, Medical College, and Specialist (Senior) in Surgery, Madras, is appointed Chief Medical Officer, Delhi, with effect from the afternoon of the 9th March, 1940.

Lieutenant-Colonel R. F. D. MacGregor, C.I.E., an Agency Surgeon, is appointed as an Additional Medical Officer at the Irwin Hospital, New Delhi, with effect from the 10th March, 1940.

On return from leave Lieutenant-Colonel W. R. Ross-Stewart, C.I.E., resumed charge of the office of Civil Surgeon, Lahore, on the afternoon of the 16th March, 1940.

Major J. C. Drummond is confirmed in the post of Surgeon-Superintendent, Presidency General Hospital, Calcutta, with effect from the 18th May, 1939.

Major A. E. Kingston relinquished charge of his special duty at the Dufferin Hospital, Rangoon, on the afternoon of 9th March, 1940, and assumed charge of the duties of the Civil Surgeon, Magwe, on the forenoon of the 13th March, 1940.

Major A. N. Duggal to be D. A. D. P., Lahore District. Dated 21st February, 1940.

Major A. N. Chopra, Superintendent, Central Jail, Jubbulpore, is appointed temporarily as Additional Assistant Director-General, Indian Medical Service, with effect from the forenoon of the 20th March, 1940.

Major H. S. Smithwick has been appointed Civil Surgeon, Belgaum, with effect from 5th April, 1940, *vice* Lieutenant-Colonel B. Z. Shah, retired.

Major F. H. Whyte is appointed to the post of Civil Surgeon, Simla West, with effect from the forenoon of the 22nd April, 1940.

*Transfers to Civil employment*

Captain W. H. G. Reed. Dated 1st February, 1940.

Major A. K. M. Khan. Dated 22nd February, 1940.

Captain W. W. Laughland. Dated 24th February, 1940.

Captain T. C. McD. Morrison. Dated 27th February, 1940.

Captain E. H. Lossing made over charge of the Hooghly Jail to Lieutenant-Colonel H. E. Murray, on the afternoon of the 12th February, 1940.

Captain J. A. M. Cameron to be Specialist in Surgery, Karachi. Dated 22nd February, 1940.

On relief of his duties in the Military Department, Captain T. M. Williams has been posted on general duty at the Bai Motlibai and Sir D. M. Petit Hospitals, Bombay, with effect from the forenoon of 10th March, 1940.

On relief of his duties in the Military Department, Captain T. C. McD. Morrison has been posted as Civil Surgeon, Sholapur, with effect from the 28th March, 1940, *vice* Major H. S. Smithwick transferred.

*To be Captain (on probation)*

Shri Rameshwar. Dated 5th March, 1940, with seniority from 5th March, 1936.

On relief of his duties in the Military Department, Captain W. W. Laughland has been placed on general duty at the Central Mental Hospital, Yeravda, with effect from the forenoon of 29th February, 1940.

On transfer from Jhelum Captain C. F. Garfit assumed charge of the office of Civil Surgeon, Murree, on the 1st April, 1940.

On transfer from Ambala Captain D. W. Taylor assumed charge of the office of Civil Surgeon, Dalhousie, on the 1st April, 1940.

*To be Lieutenants (on probation)*

Dated 1st February, 1940

Lakshman Nandkeolyar.

Brij Lal Kapoor.

## LEAVE

Major R. A. Wesson, Civil Surgeon, Gorakhpur, on 4 months' leave *ex-India* from 26th March, 1940, with permission to prefix Easter and Holi holidays.

Captain E. H. Lossing, Civil Surgeon, Hooghly, is granted leave on average pay for 3 months in India, with effect from the date on which he was relieved.

## PROMOTION

*Lieutenant-Colonels to be Colonels*

R. V. Martin, C.I.E. Dated 11th November, 1939, with seniority from 26th January, 1936.

A. C. L. O'S. Bilderbeck. Dated 24th November, 1939, with seniority from 31st July, 1936.

*Brevet-Colonel to be Colonel*

J. W. Vanreenen, O.B.E. Dated 29th January, 1940, with seniority from 31st July, 1936.

The following I. M. S. Officers have been advanced to the higher position of their rank, that is to the list of Lieutenant-Colonels selected for increased pay for ability and merit, with effect from the dates noted against them:—

Lieutenant-Colonel M. L. Treston. Dated 6th October, 1939.

Lieutenant-Colonel C. de C. Martin. Dated 8th November, 1939.

*Lieutenant to be Captain*

A. N. Roy. Dated 20th March, 1940.

## RETIREMENTS

Lieutenant-Colonel B. Z. Shah. Dated 5th April, 1940.

Captain H. L. Khosla. Dated 11th February, 1940.

## Notes

## STIBOPHEN

BURROUGHS WELLCOME AND COMPANY, to meet the demand for the English product, announce the manufacture and issue of Stibophen by licence under the Patents, etc., Emergency Act, 1939, relative to the English Patent No. 376346, the objective substance of which is Fouadin (Stibophen).

Stibophen is a trivalent antimony compound of sodium pyrocatecholdisulphonate; it is indicated in the treatment of schistosomiasis, oriental sore and granuloma venereum.

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## FOR THE TREATMENT OF SYPHILIS

THE manufacturers of N.A.B.—novarsenobillon—have sent us a copy of their new publication on this product in the treatment of syphilis.

N.A.B.—novarsenobillon—which is now more widely employed than any other arsenical throughout the Empire, is indicated in primary, secondary and tertiary somatic syphilis. Twenty-three years of consistent use, have established the position of this product so firmly that a complete revisal of the previous publication has been considered unnecessary. Certain modifications,

however, have been made where recent experience has shown them to be desirable, so that the medical practitioner using N.A.B.—novarsenobillon—may have access to the latest information available.

Copies of this book will, we understand, be forwarded gladly to any member of the medical profession on request to:—Messrs. May and Baker (India), Limited, 11, Clive Street, Calcutta, India.

## UROPAC—FOR INTRAVENOUS UROGRAPHY

THE organic iodine compound mainly used as a contrast medium in intravenous urography and other radiographic investigations is now being manufactured in Great Britain by Messrs. May and Baker, Limited, under the registered name of uropac.

This preparation—the disodium salt of 3:5-di-iodo-4-pyridoxyl-N-methyl-2:6 dicarboxylic acid—is low in toxicity and the rapidity with which it is excreted by the kidneys ensures complete safety in use. Previous to the outbreak of war the drug was not produced in Great Britain. In the form of uropac, supplies of it are now available to meet immediate demands.

A specimen of the uropac booklet has been sent to us by Messrs. Pharmaceutical Specialities (May and Baker), Limited, Dagenham, England. We understand that a copy will be forwarded to any member of the medical profession on request to:—Messrs. May and Baker (India), Limited, 11, Clive Street, Calcutta, India.

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## Original Articles

### REPORT ON TWENTY-FOUR CASES OF TROPICAL MACROCYTIC ANÆMIA IN PUNJABI MEN

By GEOFFREY F. TAYLOR, M.A., M.R.C.P. (Lond.)  
MAJOR, I.M.S.

Professor of Clinical Medicine, King Edward Medical College, Lahore

and

S. S. MANCHANDA, M.B., B.S.

House Physician, West Medical Ward, Mayo Hospital, Lahore

TROPICAL macrocytic anæmia is fairly common in the Punjab. This report is based on twenty-four cases investigated in the West Medical Ward of Mayo Hospital, Lahore, during the last six months. The cases have many points in common with those reported by Wills, Napier and Hamilton Fairley.

#### Ætiology

1. *Poverty and diet.*—The cases occurred in men of the poorest class between the ages of 25 and 60 years, whose diet was of very low quality lacking proteins, fat and vitamins. It consisted mostly of whole wheat *chapati* and pulses (*dāl*). Occasionally a little milk, meat and fresh vegetables and fruits were eaten by some of the men and in some, rice was eaten instead of *chapatis*. It was not possible to investigate the diet more fully as the cases were not investigated in their own homes, and the individual items of their diet could not be weighed. The same type of anæmia is common in Punjabi women of this class, and we propose to report on this pregnancy macrocytic anæmia at a later date.

2. *Ankylostomiasis.*—In twenty cases ova of ankylostoma were present. A count of the number of ova was not done, but the infection in some cases was severe and in others mild, as judged by the number of ova present on microscopical examination of the stools. We are investigating by egg counts the severity of ankylostomiasis infection of cases now admitted into the wards.

3. *Malaria.*—In twelve there was an enlargement of the spleen which was attributed to malaria. In fifteen of them there was a history of malarial fever.

4. *Diarrhœa.*—Diarrhœa was a prominent symptom in twelve cases and in four of these there was a history of blood and mucus in the stools. The stools were sprue-like in character in three.

5. *Syphilis.*—The Wassermann reaction was positive in two cases.

We conclude that the chief ætiological factor is a poor diet, in which there is a deficiency of either Castle's extrinsic factor, or of some other independent hæmopoietic principle, as suggested

by Napier. We will discuss the evidence for this independent principle later. The contributing factors are a loss of blood by ankylostomiasis infection and destruction of blood by malaria. Lack of absorption of the blood-forming substances caused by diarrhœa was a factor in half of our cases. Obviously the first and last factors are the important ones, namely, poor diet and diarrhœa, as ankylostomiasis and malaria do not cause macrocytic anæmia by themselves.

#### Clinical findings

1. *Blood picture.*—There was a macrocytic anæmia in all our cases. The lowest blood count showed 690,000 red cells per c.mm., while five had red cell counts below one million and eleven others had red cell counts between one and two million. The lowest hæmoglobin reading was 2.22 grammes (12.8 percentage of Sahli's scale) while ten cases had hæmoglobin less than 2.94 grammes (17 per cent Sahli's scale) and twelve others had hæmoglobin between 2.94 and 5.88 grammes (17 to 34 per cent Sahli's scale).

The highest colour index was 1.6. The highest reading on Eve's halometer was  $8.4\mu$ . The estimation of average cell volume was not done. In ten of the cases the white cell count was under 5,000, the lowest being 3,125 per c.mm. Anisocytosis and poikilocytosis of a severe degree was noted in some. The highest reticulocyte count on admission was 3.5 per cent.

2. *Van den Bergh reaction.*—In seventeen cases the van den Bergh indirect reaction was positive and in the remaining ones it was negative. The highest icteric index was 5.8, which is within normal limits, showing that there was no severe hæmolysis.

3. *Gastric test meal.*—There was complete achlorhydria after a porridge meal in two of the cases but only one of these was without hydrochloric acid after histamine injection. The others showed varying quantities of hydrochloric acid.

4. *Estimation of vitamin C.*—This was done in some cases but we are unable to come to any definite conclusion as yet.

5. *Sternal puncture.*—Sternal puncture was done in nineteen cases. In eleven of these the normoblasts were above the normal 25 per cent for Indians (Napier and Sen Gupta, 1938). The highest figure recorded was 55.6 per cent.

In eight cases the megaloblasts were above the normal 1.5 per cent, the highest reading being 12 per cent. The other counts in these eight cases were—2.5, 2.5, 3.0, 3.0, 3.5, 5.0, 7.0 and 12.0 per cent.

They all showed the ordinary signs of severe anæmia, such as pallor and breathlessness. There was a varying degree of œdema in thirteen of them. Eight cases gave a history of soreness of the tongue. There was evidence of glossitis in seven and in the others the tongue was normal. There was severe pyorrhœa in eight cases.

There were no other prominent symptoms and none had very abnormal pigmentation of the skin. There were no signs of involvement of the nervous system.

#### Post-mortem findings

One only of these men died and we were fortunate to obtain permission to perform a post-mortem examination. The patient was a man of 60 years of age, who was admitted into the hospital in September 1939, with the complaint of weakness, and pain in the abdomen and chest. He had the usual appearance of a patient with severe anaemia. The red cell count on admission was 1,000,000 per c.mm., and the hæmoglobin was 3.2 grammes per cent (19 per cent Sahli's scale). The average size of the red cells recorded by Eve's halometer was  $8\mu$ . The van den Bergh reaction was negative, and there was no urobilin in the urine. Gastric analysis showed a normal curve after a porridge meal. Sternal puncture gave the following results:—

	Neutrophils	Eosinophils	Basophils	
Polymorphonuclears	15.0	..	..	A.
Metamyelocytes ..	44.0	..	..	
Myelocytes ..	15.0	..	..	
Premyelocytes ..	8.5	0.5	..	
Myeloblasts ..	..	..	..	B.
Lymphocytes ..	1.0	..	..	
Monoocytes ..	..	..	..	
Normoblasts ..	12.0	..	..	
Erythroblasts ..	3.5	..	..	
Megaloblasts ..	0.5	..	..	
Ratio of A to B	5	1		

Hookworm ova were present in the stools in large numbers. He was in the wards for 10½ weeks and was treated by liver injections (Exatrope injections 2 c.cm., on alternate days) and yeast extract by the mouth. The ankylostomiasis was treated by carbon tetrachloride and oil of chenopodium. The blood picture and general condition improved only slowly and rose to 1,560,000 red cells per c.mm., and 4.84 grammes of hæmoglobin (28 per cent Sahli), the colour index being 1.14 and the average size of red cells  $7.7\mu$ , which is slightly macrocytic. He died suddenly while sitting up in bed, presumably from sudden myocardial failure. The post-mortem examination showed some free fluid in the abdomen and a recent ulcer two inches from the pylorus in the duodenum. The bone marrow was yellow-grey in colour, soft and fatty in consistency, both in the shafts and ends of the bones. The bone marrow was thus aplastic as judged by naked-eye appearance. Unfortunately sections of it were not prepared.

This case is of interest because it shows that the lack of response to treatment is associated with and is probably caused by aplasia of the bone marrow. Except for the lack of response to treatment there appears to be no method of judging the aplastic condition of the marrow. In this case the sternal puncture readings were within normal limits, and we cannot see how examination of sternal puncture material will help in diagnosing this aplasia. Possibly the absence of a normoblastic or megaloblastic reaction in the bone marrow may indicate an aplastic state, but this is not confirmed by findings in other cases noted below.

It is also of interest in showing a slightly macrocytic blood picture and aplasia of the marrow.

#### Response to treatment

Owing to the severity of the condition of many of the cases we treated them by both marmite and yeast extract by the mouth and by liver

injections. Because of the war, purified concentrated liver extracts could not be obtained and Exatrope (Glaxo) and Erythgen (Carnrick) were used. Blood transfusion was done in two cases only. We did not employ it more frequently because during the last few years there have been several deaths following blood transfusion in cases with severe anaemia in this hospital. We are now using small transfusions, repeated frequently, of not more than 200 c.cm. at a time.

Owing to the severe condition of many of these cases we did not feel justified in withholding liver injections in order to enable us to note the response to marmite alone. Most of the cases of ankylostomiasis were treated at once with carbon tetrachloride and oil of chenopodium and we noted no toxic effects of these drugs. Thymol did not appear to be as efficient. All cases were put on the hospital diet consisting of milk, *chapati*, meat, fresh fruit and vegetables when they were able to eat it.

The highest reticulocytosis noted after treatment had begun was 25 per cent.

Seven of the cases improved only slowly with treatment. Eleven others improved rapidly within a few weeks, while five left the hospital against our advice before treatment had been completed.

The sternal puncture findings of the cases which improved slowly, were normal in three, but two showed a normoblastic reaction with normoblasts up to 55.6 per cent and 37.6 per cent, and one other case showed 2.5 per cent megaloblasts which is slightly above the normal limit of 1.5 per cent. We suggest that the bone marrow of these cases was in a partially aplastic condition because of their lack of response to treatment.

In seven of the cases the average size of the red cell and the colour index remained above normal after more than one month's treatment. In two of these cases the anaemia was macrocytic after two and three months respectively. We do not understand the reason for this, as both had intensive treatment by liver injections, marmite by the mouth, and blood transfusion.

#### Discussion

The findings in these cases appear to be similar to those of macrocytic tropical anaemia reported in other parts of the world. The blood picture and sternal puncture findings have been examined in order to try to find some differences between the findings of tropical macrocytic anaemia and those of Addison's pernicious anaemia. There appears to be no difference in the blood and sternal puncture material except that it is said that hæmoglobinized megaloblasts occur in Addison's anaemia only. We have not seen any of these cells in the sternal puncture material of these cases. But apart from this we can find no difference. In both conditions the anaemia may be very severe, a high degree of macrocytosis and nucleated red cells may be

Table of sternal puncture count on admission

Case number	POLYMORPHO-NUCLEARS			METAMYELOCYTES			MYELOCYTES			Premyelocyte	Myeloblast	Lymphocyte	Monocyte	Normoblast	Erythroblast	Megaloblast
	Neutrophil	Eosinophil	Basophil	Neutrophil	Eosinophil	Basophil	Neutrophil	Eosinophil	Basophil							
1	15.0	..	0.3	44.0	..	0.6	15.0	0.5	..	8.5	..	1.0	..	12.0	3.5	0.5
2	7.6	..	..	18.3	..	..	8.0	..	..	0.3	..	9.0	..	55.6	5.3	0.3
3	5.0	0.3	..	32.0	..	..	6.5	..	..	7.0	0.6	1.0	..	37.6	8.3	1.0
4	9.0	1.5	..	26.0	0.5	..	14.0	..	..	23.0	..	1.0	..	15.6	7.9	2.5
5	10.5	1.5	..	15.0	1.0	..	18.0	..	..	3.0	0.5	..	..	27.0	9.0	12.0
6	5.1	0.2	..	39.2	..	..	12.3	..	..	6.0	0.5	1.0	..	12.5	15.0	7.0
7	17.0	0.4	..	37.6	..	..	9.3	0.8	..	0.4	..	2.0	..	31.6	2.4	0.4
8	6.0	..	..	47.5	0.5	..	22.5	..	..	0.5	..	0.5	1.0	21.0	0.5	..
9	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
10	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
11	25.0	..	..	30.0	2.0	..	7.0	..	..	0.5	..	..	..	24.0	8.0	3.5
12	17.0	..	..	30.0	..	..	17.9	..	..	8.0	..	2.0	..	20.4	3.5	1.2
13	12.0	0.6	..	39.0	1.4	..	12.0	0.2	..	0.4	..	2.0	0.4	25.0	4.0	3.0
14	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
15	9.0	..	..	34.3	0.3	..	14.6	..	..	0.6	..	..	1.0	36.6	2.6	0.6
16	3.4	..	..	23.0	..	..	32.0	..	..	3.0	..	..	..	26.5	7.0	3.0
17	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
18	27.0	..	..	13.0	1.0	..	13.0	..	..	..	..	3.0	..	38.0	4.0	1.0
19	11.0	3.0	..	21.5	..	..	16.0	..	..	6.5	..	1.5	..	37.0	2.0	1.5
20	15.0	..	..	27.0	2.5	..	15.0	..	..	14.5	..	2.0	..	19.5	3.0	1.5
21	16.7	0.7	..	20.0	0.3	..	25.3	0.7	..	..	..	5.6	..	20.0	5.3	5.0
22	25.0	..	..	25.5	..	..	10.0	..	..	6.0	0.8	2.0	..	27.0	3.7	0.0
23	2.0	0.5	..	37.5	..	..	19.0	..	..	3.5	..	..	..	32.5	2.5	2.5
24	16.0	1.5	..	25.0	0.5	..	9.0	..	..	1.5	..	1.0	..	33.0	10.0	1.0

Table of blood findings on admission

Serial number	R. B. C.	W. B. C.	Hb. in grammes, per cent	Diameter of red cell in $\mu$	van den Bergh	Icteric index	Reticulo-cyte count, per cent	Colour index
1	1,000,000	8,125	3.04	8.0	Negative	..	1.0	1.1
2	1,760,000	4,260	7.26	7.9	Indirect +	4.0	1.0	1.3
3	1,200,000	4,200	5.2	7.8	Do.	4.0	3.0	1.25
4	790,000	4,800	2.7	8.4	Do.	5.3	..	1.2
5	1,820,000	4,600	6.9	7.8	Do.	4.8	2.5	1.3
6	770,000	3,225	4.15	8.2	Do.	5.0	2.0	1.5
7	2,320,000	6,250	10.3	8.1	..	2.3	3.0	1.3
8	2,430,000	6,250	9.3	8.19	Indirect +	3.5	..	1.1
9	3,330,000	5,600	12.9	8.2	Do.	3.0	..	1.1
10	690,000	5,000	3.6	8.1	Do.	3.5	3.5	1.6
11	2,070,000	5,625	7.2	7.8	Do.	2.0	..	1.06
12	1,700,000	8,200	6.05	7.8	Do.	4.0	..	1.1
13	2,420,000	5,200	10.4	7.8	Do.	..	..	1.5
14	1,170,000	3,750	5.1	8.19	Negative	..	..	1.4
15	1,190,000	4,100	4.3	7.81	Indirect +	3.5	..	1.1
16	2,200,000	3,125	8.6	8.4	Negative	2.2	2.5	1.25
17	2,960,000	4,960	10.3	7.8	Indirect +	2.1	..	1.03
18	1,250,000	7,400	5.1	7.84	Negative	..	3.5	1.2
19	1,160,000	4,375	4.3	7.8	Indirect +	3.6	7.5 (3 weeks after admission).	1.1
20	1,200,000	3,775	6.9	8.19	Do.	5.0	1.5	1.6
21	1,660,000	4,235	6.9	8.0	Do.	..	2.5	1.25
22	1,280,000	5,000	6.9	8.2	Negative	..	0.66	1.4
23	860,000	6,875	4.1	8.0	Indirect +	5.0	..	1.25
24	1,700,000	4,750	6.05	7.9	Do.	5.0	1.0	1.02

found in the peripheral blood, anisocytosis and poikilocytosis may be marked. The sternal puncture material may show a megaloblastic or normoblastic reaction or it may be normal. Blood destruction, as judged by the van den

Bergh reaction and icteric index, may be more severe in Addison's anæmia.

If Castle's theory of the extrinsic and intrinsic factors forming a hæmopoietic principle be  
(Continued at foot of next page)

adrenals that we have observed in the study of about two thousand autopsies from the year 1919 to March 1940. The following table shows the results of our investigation :—

TABLE

Total number of autopsies studied	Total number of supra-renal abnormalities	Nature of abnormalities in the gland	Total number of cases showing extensive tuberculous lesions in the body
2,007	16	(a) Tuberculosis .. 2 (b) Tumour— primary .. 1 secondary .. 1 (c) Hæmorrhage .. 2 (d) Congestion .. 8 (e) Actinomycosis— secondary .. 1 (f) Degeneration and hæmorrhage .. 1	352

From the above number the following seven cases are described in detail in consideration of the rare and interesting nature of the lesions.

*Case 1.*—M. B., female, aged 30, was admitted into the hospital on 9th August, 1938, in the following condition—

The patient complained of intense epigastric pain which was of about four months' duration. On examination pulse rate was found to be 170 per minute with very feeble volume. There was rigidity and tenderness of the abdomen especially over the pelvic region. A hard and tender mass was felt in the right iliac fossa. She died within a few hours of admission and an autopsy examination, which was done the next day, showed the following:—

A pint of blood-stained purulent fluid in the peritoneal cavity. Omentum was extensively adherent to the pelvic organs; tubo-ovarian masses were seen on both sides with extensive adhesions and fibrinous deposits. These masses, when cut, showed frank pus which yielded *B. coli* on culture. A tumour mass was seen above the left kidney. The other regions showed no marked change. Opinion as to the cause of death was peritonitis following ruptured suppurative tubo-ovarian mass. The tumour in the kidney region was found to arise from the left suprarenal gland, and it was globular in shape and pinkish in colour, somewhat cystic in feel and it measured 12½ by 6 inches. The tumour completely replaced the adrenal tissue of which a strip of cortical portion could be seen at the periphery of the tumour. On cutting through the mass the tumour was found to consist of partly solid and partly soft tissues which were of different colour at different places—red, hæmorrhagic, pale, brown and dirty greenish black (plate VI, figure 1). There was no fluid within the tumour. The entire growth was surrounded by a fibrous capsule which separated the new growth from the scanty remnant of the cortical portion of the adrenal gland.

Microscopical anatomy of the tumour—(hæmatoxylin-eosin stain and Mallory's phosphotungstic acid stain)—the growth consisted mainly of compact masses of large ganglionic cells with very little intercellular substance

(plate VII, figure 2). Nerve fibres and intercellular neuro-fibrils were scanty. On higher magnification (plate VII, figure 3) the ganglionic cells were well seen; the nuclei were usually seen to be placed at the periphery and binucleated cells were also present. The nucleoli were distinct. Most of the cells showed definite vacuolations in their cytoplasm giving a foamy appearance; evidently this is a degenerative process which has set in within the tumour. No other abnormal finding in any other region. Right suprarenal gland was normal.

*Commentary.*—The structure of the tumour was of a ganglion neuroma. Tumours arising from the sympathetic nervous system are not common (Geschickter, 1935) and in the reported cases the tumours had their origin in the central nervous system, cranial nerves and their roots and ganglions, neck, thorax, alimentary tract, suprarenals, retroperitoneal region, pelvis and the peripheral nerves. Ganglion neuromas from the suprarenals are still rarer. McFarland (1931) collected about one hundred cases of this type of new growth of which only thirteen had their source in the adrenal gland. These tumours usually run a benign course although rarely they may take a malignant turn. Extensive destruction of the adrenal substance by neoplasm may give rise to Addison's disease syndrome. In Guttman's (1930) series of 566 cases of Addison's disease only 1.2 per cent was due to a neoplastic condition of the suprarenal. In this case there was practically no suprarenal substance left excepting a small strip of cortex, which was for practical purposes devoid of any function. Though the destruction was extensive there were no symptoms of suprarenal failure, probably because the right suprarenal was healthy but it showed no compensatory hypertrophy.

*Case 2.*—J. H., male, aged 51, admitted into the hospital on 2nd August, 1939, with the following complaints:—

- (1) Generalized weakness and lassitude, progressive anæmia and loss of weight.
- (2) Vomiting after meals—duration four months.
- (3) Pain during swallowing behind the sternum and in the epigastrium, left lumbar and left iliac regions.

*History.*—About a year prior to his admission, the patient was suffering from 'acidity' and he felt he was getting weaker. About eight months back he felt difficulty in swallowing but took no notice of it. Since four months he started bringing up all food immediately after eating and about that time he began to feel occasional painful sensations in the left iliac region and chest.

*Condition on admission.*—Poorly nourished, moderately built, looked markedly anæmic. There was no jaundice and the temperature was normal; P/R = 80/20; blood pressure—systolic 115, diastolic 70.

#### EXPLANATION OF PLATE VI

Fig. 1. *Case 1.*—Exact size of tumour (cut surface). Note the different colours at different areas and a small rim of suprarenal structure at the periphery.

Fig. 6. *Case 3.*—Both suprarenals showing the hæmorrhagic appearances of the organs. The pale areas are composed of degenerated glandular elements.

Fig. 11. *Case 6.*—Suprarenal glands showing the gross appearance; both the glands have been partially cut open to show yellowish-grey nature of the necrotic change.

Fig. 1.

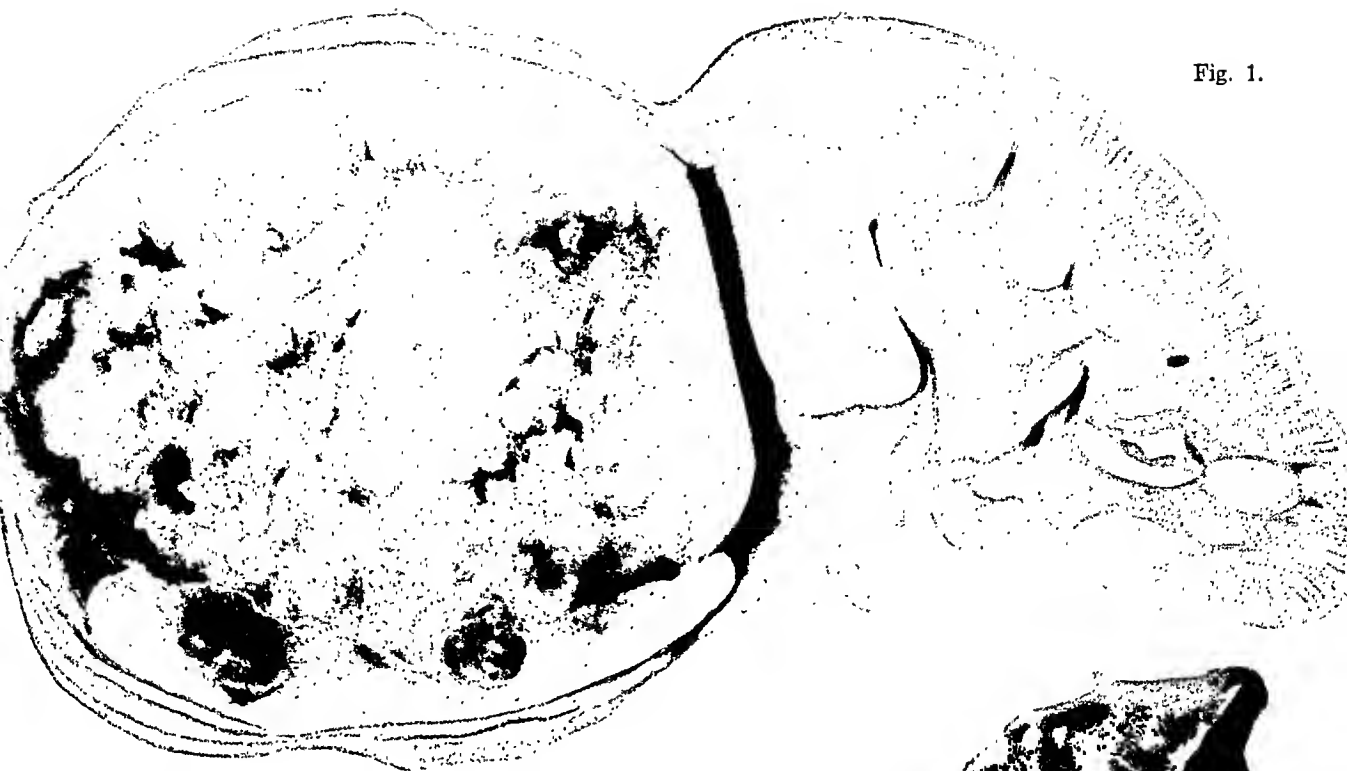


Fig. 6a.



Fig. 6b.



Fig. 11a.

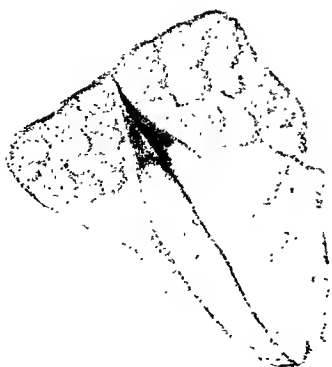
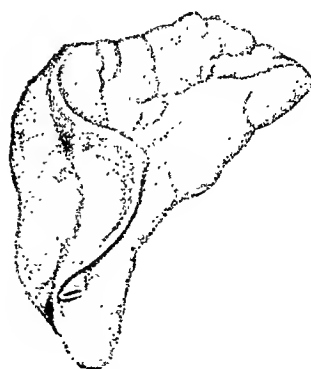


Fig. 11b.







*After admission.*—X-ray examination showed a new growth of the cardiac end of the stomach. A laparotomy was performed and a huge hard growth with uneven surface was found occupying the fundus and body of the stomach.

The patient died on 7th September, 1939, and a partial post-mortem was done to explore the abdominal cavity. Besides the gastric growth a number of huge masses were seen within the peritoneal cavity. These were removed and on examination showed extensive neoplastic involvement of the stomach. A mass 3 by 3½ inches was seen at the hilum of the right kidney but separate from it; another mass the size of a ping pong ball was seen just below the greater curvature of the stomach near the pylorus, but quite separate from it. A third mass, measuring 3 by 2 inches was noticed just above the left kidney (plate VIII, figure 4). On histological examination the gastric growth showed the structure of an adenocarcinoma; masses below the stomach and near the right kidney showed the structure of lymphatic glands infiltrated with adenocarcinomatous process. The mass just above the left kidney was found to be the left suprarenal, which was extensively infiltrated with the same tumour. On examining a number of blocks from the left suprarenal it was seen that very little of the adrenal structure was left. The entire growth consisted of adenocarcinoma with very scanty adrenal tissue here and there (plate VIII, figure 5).

*Commentary.*—Gastric carcinoma has a wide metastatic spread but infiltration into the suprarenals is rare (Ewing, 1931). The lymphatic spread of this tumour is obvious from the microscopic picture of the abdominal lymphatic glands but there must have been hæmatogenous spread also because otherwise the suprarenal metastasis cannot be explained. The extensive suprarenal involvement, which has almost entirely replaced the gland structure, must have been of long duration, putting the gland out of function for some time. The right suprarenal was not available.

*Case 3.*—J. M., male, aged 40, admitted into the hospital on 28th February, 1939, with the following history:—

Asthma for the last 12 years; extreme difficulty in breathing for about 24 hours. On examination signs of cavitation at the apex of the right lung were detected and a diagnosis of pulmonary tuberculosis was made. He died on 6th March, 1939, and the autopsy examination showed bilateral plastic pleurisy and emphysematous condition of both lungs. Right lung showed two cavities at the lower part of the base and miliary tubercles in the whole of the lower lobe. Left lung showed consolidation at the base. Liver was congested and enlarged. Spleen was congested. Both the suprarenals were palpably enlarged, the right one being the larger. No other gross abnormality was detected. The enlarged suprarenals were then studied. They felt hard; on cutting through, the glands were found to be hæmorrhagic looking with pale yellowish areas within (plate VI, figures 6a and 6b). The consistency was homogeneous.

*Microscopical examination.*—The normal pattern of the gland was completely disorganized and the cortical and medullary areas could not be differentiated. The gland structure showed marked degeneration; the shadow cells taking only eosin stain (plate IX, figure 7). The degenerated areas were filled with red blood cells. At some areas these hæmorrhages showed signs of organization and at other places isolated islets of atrophied cortical structure could be detected interspersed with masses of red blood cells and young fibroblasts (plate IX, figure 8). No signs of any inflammation nor caseation could be seen anywhere. These changes were more or less in all parts of both the organs.

*Commentary.*—The case presented a condition of widespread degenerative changes of the glandular structures and its infiltration with blood. These bilateral changes in the suprarenal were found in a case of active pulmonary tuberculosis. The initial change seemed to be essentially a degenerative one with subsequent hæmorrhage into the substance resulting in the gross increase of the size of the organ. Guttman (1930), while discussing the rôle of degenerative changes of the adrenals in the causation of Addison's disease, pointed out the rare possibility of tuberculosis as the ætiologic factor of the degeneration. In the present case, though associated with active pulmonary tuberculosis, the suprarenal itself showed no caseation or any picture to suggest a tuberculous process. Our figure 7 is very similar to some of the pictures produced by Guttman, viz, degeneration of the gland substance which is infiltrated with red blood cells but the case reported by Guttman showed the organs to be small and thin.

*Case 4.*—C. C. P., male, aged 60, was admitted into the hospital on 27th February, 1940, in the following condition:—

Unconsciousness with flaccid paralysis of the right upper and lower limbs, contracted pupils, blood pressure 165/115; pulse 100, respiration 28. A diagnosis of cerebral hæmorrhage was made. A week later the patient died; on post-mortem examination the following findings were made—extensive hæmorrhage in the left corpus striatum, hypostatic pneumonia, hypertrophied left ventricle and marked atheroma of the aorta. The left suprarenal was enlarged about twice the normal size. The right suprarenal was normal. On examination, left suprarenal was found to be purpled in appearance, the normal cream colour being absent. On cutting through the organ it was found to be frankly hæmorrhagic. Histological examination showed that the structural units were present but there was enormous congestion and at places free red blood cells were found scattered within the gland substance. This hæmorrhagic condition was so marked that in most of the blocks studied the glandular element was seen as islets in the midst of masses of red blood cells (plate X, figure 9). There were no degenerative changes in the adrenal tissue but the usual normal arrangement was lost.

*Commentary.*—This is a case of senile cerebral hæmorrhage with associated suprarenal hæmorrhage. It seems probable that the factors which were responsible for the cerebral lesion caused the adrenal damage too, viz, vascular sclerosis.

*Case 5.*—A. R., aged 35, male, admitted on 30th March, 1928, with the following complaints:—

- (1) Frequent motions, about ten times in 24 hours—duration a month and a half.
- (2) Pain in the hypogastric region before and after the motions—the same period.
- (3) General wasting.
- (4) Fever, daily rise of temperature up to 102°F. for a month.

*History.*—About a year ago he had an attack of a similar nature, viz, loose motions seven or eight times daily for one month, with fever and cough. After a month he got over the attack which recurred after a month and a half and for which he went to hospital. A diagnosis of pulmonary tuberculosis was made. In the hospital he continued to have the loose motions and fever. Blood examination showed secondary type

of anaemia, formaldehyde test was positive. Stool examination showed no significant findings.

He died on 3rd July, 1928, and an autopsy showed advanced pulmonary tuberculosis a short summary of which was published (De and Chatterjee, 1934) but no detailed description of the suprarenal was noted. The left suprarenal gland was found to be grossly involved in a suppurative process. The organ was not much enlarged but appeared nodular. On cutting through the substance it was found to be composed mainly of suppurative material which almost completely filled the gland. On histological examination the characteristic appearances of actinomycotic infection (plate X, figure 10) were seen. Very little gland structure was present. Actinomycotic foci were present in a sinus on the left upper arm and the left kidney showed extensive actinomycotic involvement.

*Commentary.*—The actinomycotic invasion of the suprarenal gland was a part of the generalized actinomycotic infection accompanying pulmonary tuberculosis. The left suprarenal was evidently completely out of function; the gland did not show any compensatory reaction.

*Case 6.*—A. S., female, aged 30, was admitted into the emergency ward of the hospital on 1st June, 1938, with the following symptoms:—

Pain in the chest, cough with expectoration and fever; duration four months. She gave a history of previous hæmoptysis.

*On examination*—the patient was found to be extremely emaciated; temperature 101°F. and pulse rate 110 per minute, respiration 32 per minute. Both the lungs were full of râles and crepitations. Heart sounds were feeble but regular. A clinical diagnosis of pulmonary tuberculosis was made. She took her discharge on 3rd June. On the morning of 5th June she was found in a condition of exhaustion and was picked up by an ambulance and admitted into the hospital. The pulse was almost imperceptible and the patient was in a moribund condition. She died twenty-four hours after her re-admission. An autopsy was performed on 8th June and the following conditions were observed:—

The general appearance showed much emaciation. Both the pleural cavities were obliterated by dense adhesions. Right lung showed no gross abnormality. Left lung showed numerous cavities of varying size, which were distributed throughout the upper lobe. Extensive caseous pneumonic consolidations were found throughout the lower lobe. Left hilar lymph glands were enlarged and caseous. The small intestine at its lower part showed a number of ulcerated areas, tuberculous in nature. Adrenal glands—both the glands were enlarged; nearly half of the right adrenal was replaced by yellowish-white caseous looking areas; the left gland was also extensively involved (plate VI, figures 11a and 11b) and on section many small caseous foci were seen scattered throughout the organ. Scrapings from the lung and intestinal ulcers showed acid-fast bacilli; scrapings from the necrotic areas of the suprarenals did not show any acid-fast bacilli.

*Microscopical anatomy.*—The section of the lung showed some areas filled with large mononuclear phagocytic cells, lymphocytes, scanty fibrous tissue network, many neutrophilic polymorphonuclear and red blood cells, and other areas showed at homogeneous caseous areas. Giant cell formation was not seen; intestine—section showed typical tuberculous type of granulation tissue.

*Suprarenal*—there were large areas of coagulative necrosis destroying the gland tissue completely. The cortex and the medulla of both the organs were extensively involved with very small isolated islets of cortical substance left (plate XI, figure 12). No giant cells were seen.

*Commentary.*—The case showed bilateral tuberculous involvement of the suprarenal glands

in association with active pulmonary and intestinal tuberculous lesions. Though the destruction was extensive the case showed no obvious picture of adrenal failure.

*Case 7.*—J. R., male, aged 55, motor driver by occupation, was admitted into the hospital on 22nd February, 1940, with the following complaints:—

- (1) Difficulty in breathing—duration four years.
- (2) Palpitation—one year.
- (3) Inability to walk because of general weakness—one month.
- (4) Loss of weight.

*History.*—About five years back he had an attack of palpitation from which he suffered for about a year. It would come at about ten or twelve days' intervals and would last for about five minutes. After some treatment this trouble was relieved. After a few months of respite he began to experience difficulty in breathing off and on, which gradually increased in severity. Since the last four months prior to his admission the difficulty became very marked and the palpitation also reappeared. Because of his respiratory difficulty, palpitation and extreme weakness in walking and gradual loss of weight, he sought hospital aid. The patient had a past history of syphilis and gonorrhœa for which he was treated. He had several attacks of malaria. There was nothing particular in the family history. He was addicted to opium which he took daily. He had nocturnal sweats which sometimes were rather excessive.

*On examination.*—A man with an anxious look and gasping. There was slight cyanosis and the extremities were cold. He was orthopnoic and the difficulty was both inspiratory and expiratory in nature. There was epigastric pain and he often felt giddy. There was always a sort of sinking feeling.

*Progress in the hospital.*—The patient continued to go downhill with three main features, *viz*, extreme tired feeling, marked insomnia and dyspnoea.

*Blood report*—hæmoglobin 70 per cent, red cells 3,600,000 per c.mm., leucocytes 11,236 per c.mm., polymorphonuclears 74 per cent, lymphocytes 32 per cent, monocytes 4 per cent, eosinophils 2 per cent, sputum no acid-fast bacilli. Blood urea 40 mgm. per cent, N.P.N. 47 mgm. per cent, cholesterol 354 mgm. per cent, chloride 402.7 mgm. per cent, urine urea 0.3 mgm. per cent. The patient died on 22nd February, 1940.

*Post-mortem findings:* *Left pleural cavity.*—Recent adhesions at the apex and antero-laterally. *Right pleural cavity*—normal. Left lung was emphysematous and there were interlobar adhesions present; base cedematous and bronchioles were much dilated. *Right lung*—voluminous and cedematous. *Heart*—weight 250 gm. and flabby. *Spleen*—enlarged with capsular thickening. *Liver*—congested and blackish looking. *Gastro-intestinal tract*—no gross abnormality. *Brain and spinal cord*—no abnormality. *Thyroid gland*—no abnormality. *Right kidney*—on section a small necrotic area about  $\frac{1}{2}$  by  $\frac{1}{4}$  inch in size was seen in the medulla near the lower pole (plate XI, figure 13). *Histological sections* from the area showed the typical tuberculous nature of the lesion, *viz*, caseation and giant cell formation (plate XII, figure 14).

*Suprarenals.*—Both the organs were much enlarged, to the size of  $2\frac{1}{2}$  by 2 by  $\frac{1}{2}$  inches with marked nodular surfaces. On cutting through the glands these were found to be entirely composed of cheesy material which at places was seen broken down and a thick, creamy material escaped out of the mass (plate XI, figure 13). Both the glands showed the above picture and the normal glandular appearances were entirely absent. On histological sections—caseation was found everywhere. No giant cells were seen. The normal cortical and medullary structures had completely disappeared and in only one of the blocks a slight cortical element was seen (plate XII, figure 15).



Fig. 2.—Case 1. Low power photomicrograph of a section of the tumour. It is composed of ganglion cells and it is encapsulated by fibrous tissue. At one corner the remnants of the normal gland structure is seen.  $\times 175$ .

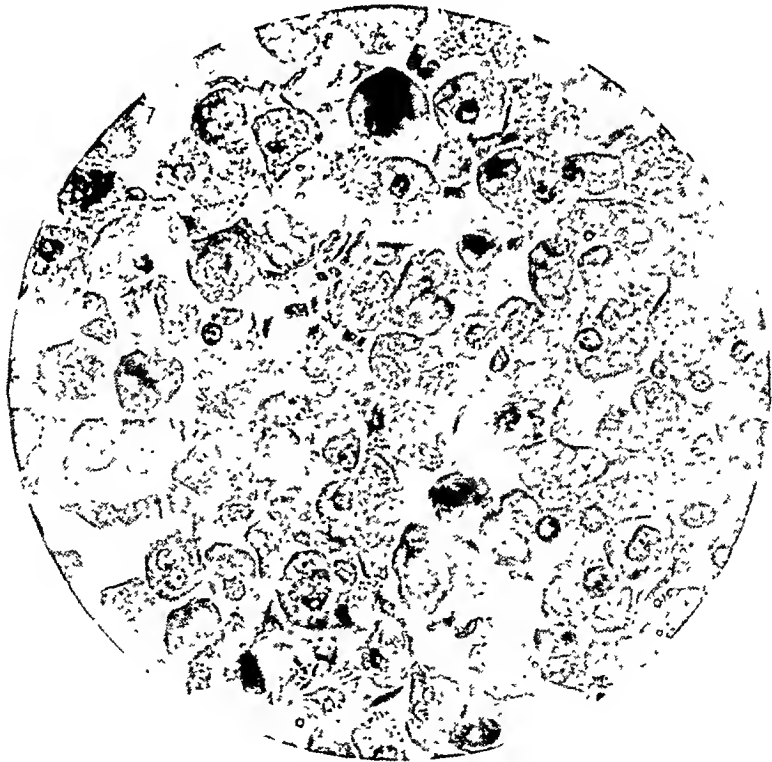


Fig. 3.—Case 1. High power photomicrographic view of the tumour cells. Note the double nuclei in some of the cells. The vacuolated appearance of the cells is apparent.  $\times 500$ .

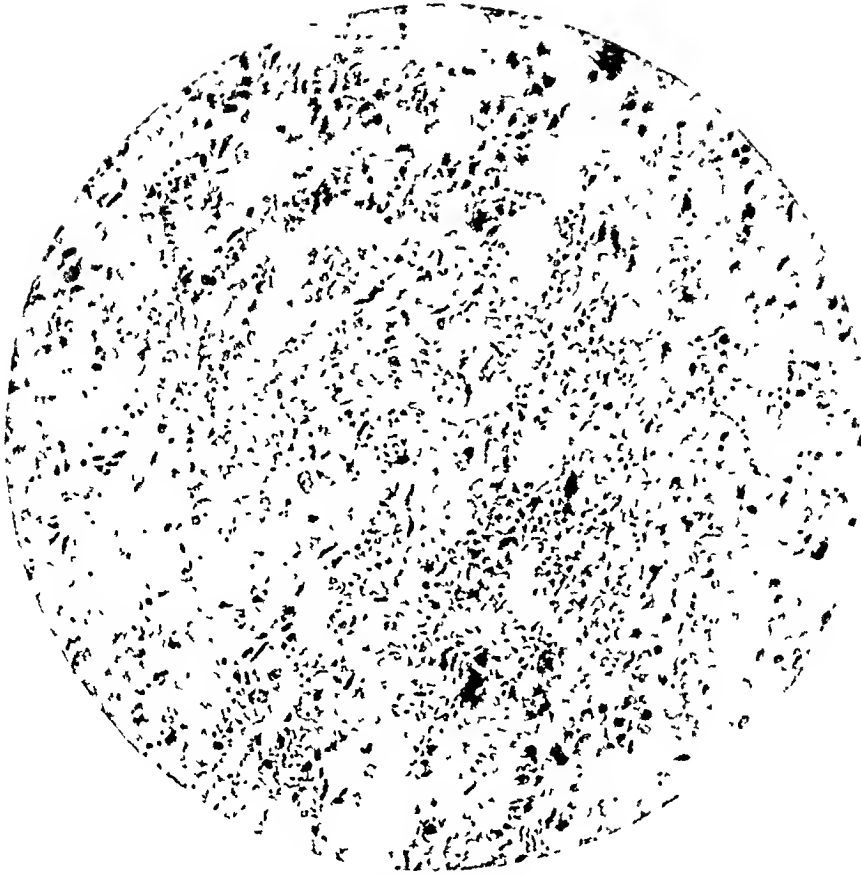


Fig. 9—Case 4 Photomicrographic view of a section of the suprarenal gland showing the congestion and hemorrhage into the gland substance  $\times 500$

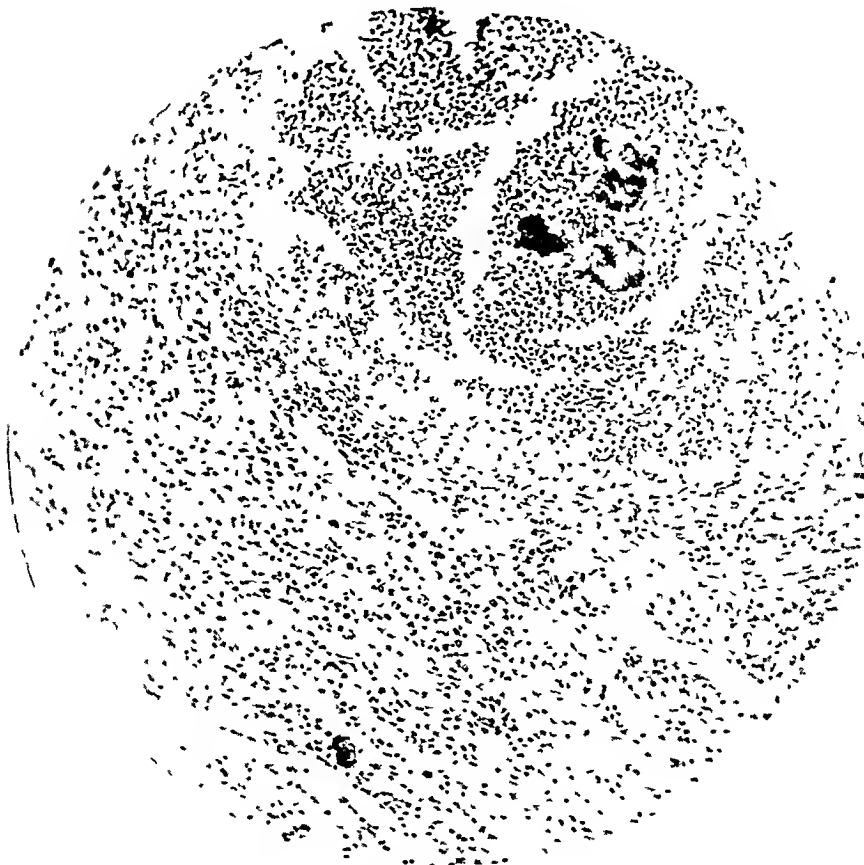


Fig. 10—Case 5 Photomicrograph of a section of a piece of suprarenal gland showing the actinomycotic foci within the gland; the leukocytic layer around the bacterial colony is well seen.  $\times 265$ .

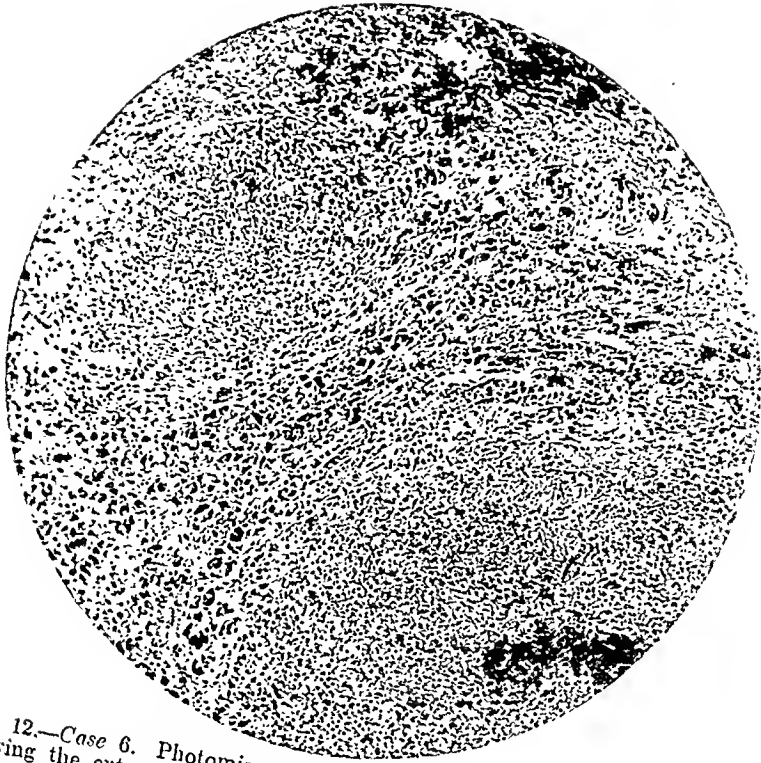


Fig. 12.—Case 6. Photomicrographic view of the suprarenal gland showing the extensive necrosis. A few altered gland cells are also seen in the field.  $\times 265$ .

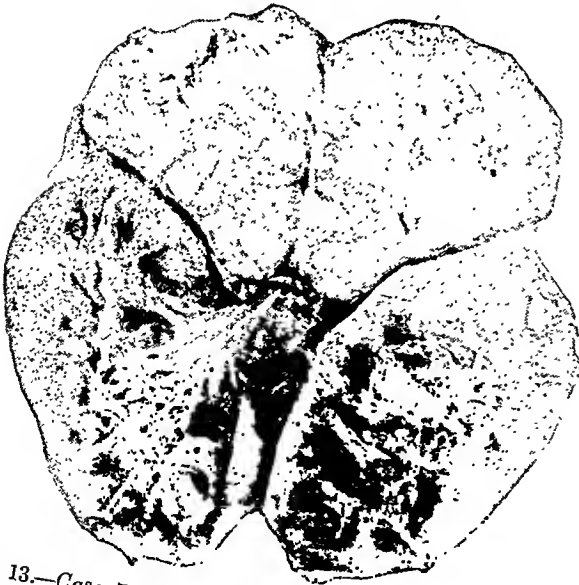


Fig. 13.—Case 7. Photograph of the left kidney with the suprarenal gland. In the medullary substance of the lower pole of the left kidney a small necrotic area is seen. The extensive involvement of the suprarenal is apparent. The other suprarenal showed similar change.

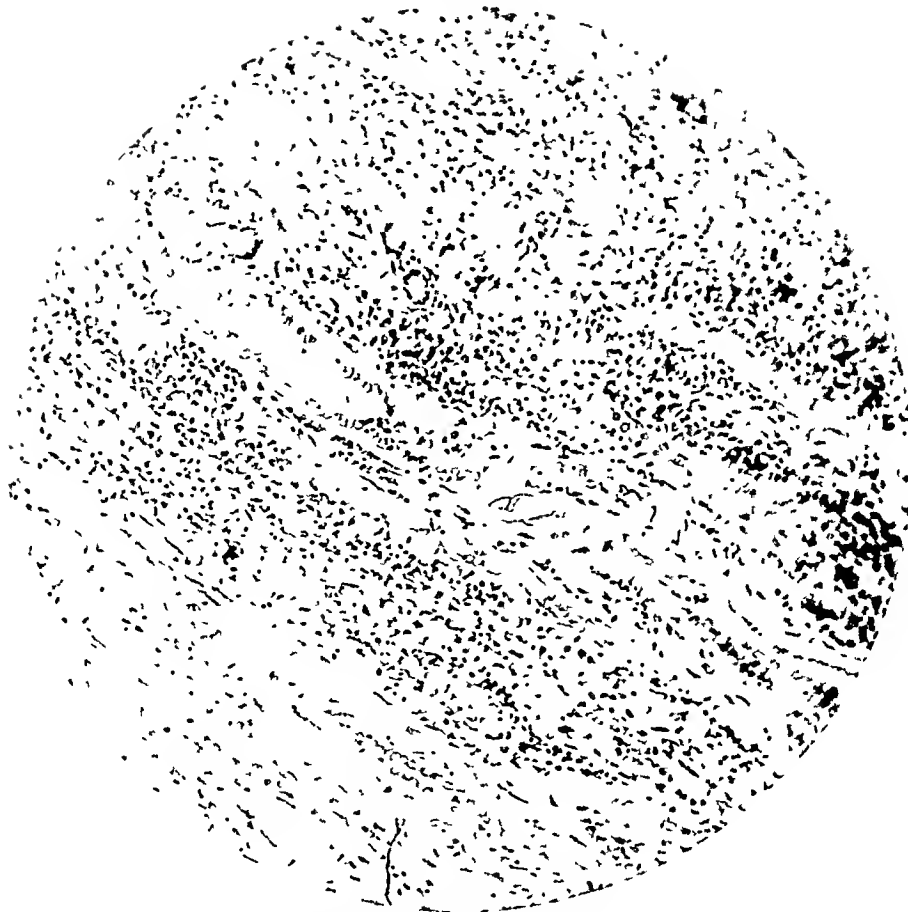


Fig. 14.—Case 7. Photomicrograph of the section of the renal tissue from the necrotic area at the lower pole of the left kidney. The typical tuberculous nature of the lesion with giant cells is well seen; some of the renal tubules which have undergone considerable structural change owing to fibrosis may also be seen.  
× 340.

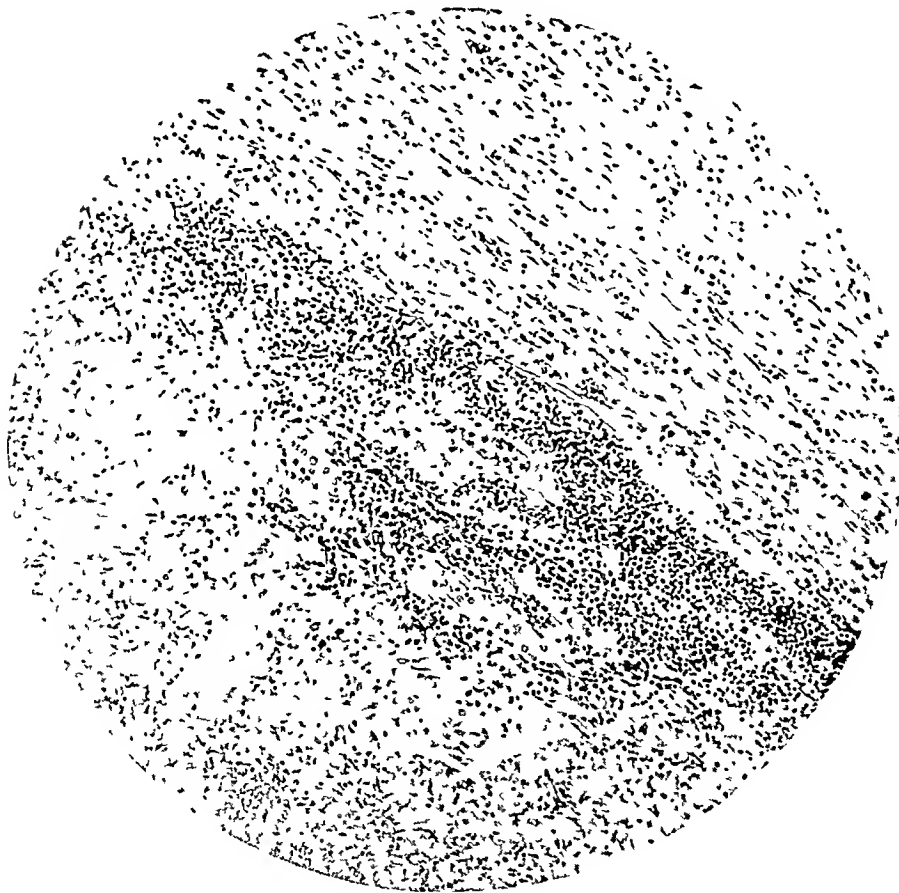


Fig. 15.—Case 7. Photomicrograph of a section from the suprarenal gland. Note the caseated area with round cell infiltration. An area of partially degenerated glandular substance is also seen.  
× 265.



*Commentary.*—Extensive bilateral tuberculous process was evident. There was no sign of tuberculous lesions anywhere else excepting the focus in the left kidney. Tuberculosis of the suprarenals is always secondary but the primary lesions may or may not be noticeable. The spread is by the hæmatogenous route. Secondary spread from the kidney is extremely rare (Boyd, 1935). In the present case the active lesion in the left kidney is in all probability the primary lesion.

*Discussion.*—The suprarenal glands are not a common site for disease. Out of two thousand unselected autopsies the organs were found to be diseased only in 16 cases. It is surprising that except in one case (case 7) none of these showed the usual signs of suprarenal failure—the Addison's disease syndrome—the characteristic pigmentation, extreme weakness, gastro-intestinal disturbances and low blood pressure. Unfortunately in the cases under review the blood pressure records were not complete and so no observation can be made on that point. Addison's disease is a rare condition. Diseased suprarenals are not necessarily associated with the Addison's disease syndrome because of the fact that a slight amount of healthy structure may be sufficient for life or an unnoticed aberrant adrenal structure might take up the function. In our series all the seven cases showed complete disorganization of one of the glands and both the glands in three cases but only in case 7 was there suggestion of adrenalin failure—gastro-intestinal disturbance and extreme weakness. Both in cases 6 and 7 bilateral destruction of the gland had existed for a long time yet neither showed the most constant characteristic, *viz*, pigmentation, although cases of Addison's disease are possible without pigmentation (Hadfield and Garrod, 1938, and Guttman, 1930).

Atrophy, tumour, syphilis, degenerative and vascular changes and tuberculosis are the usual causes of Addison's disease of which tuberculosis accounts for 70 per cent. Our table shows 352 tuberculosis cases out of two thousand autopsies (roughly 18 per cent). Out of these 352 cases the tuberculous involvement of the suprarenal occurred only in two cases (about 0.56 per cent). From the figures of different workers Guttman collected the percentages of tuberculosis of the suprarenals in association with pulmonary tuberculosis which ranged from 2 per cent to 5 per cent. In our series the figure is still smaller. Considering the prevalence of tuberculosis in Bengal the incidence of Addison's disease due to tuberculosis would be expected to be higher. Another interesting point is that in Addison's disease due to tuberculosis of the suprarenals, usually there is no manifestation of active tuberculosis anywhere else in the body. In the two cases under review one showed extensive active exudative type of tuberculosis of the lung and intestine and in the other one there was involvement of the kidneys. It is noted that because of

the rarity of Addison's disease, unless all the classical signs and symptoms are present it is not surprising that the condition might be overlooked. In both the cases 6 and 7 on autopsy, the bilateral extensive destruction was clear but neither gave any definite indication of the possibility of frank Addison's disease.

With regard to the rôle of the cortex and the medulla in the production of Addison's disease, there were long controversies in the past, but the balance of evidence at present seems to place the cortical portion as mainly responsible for the signs and symptoms, although the part played by the medulla is not altogether insignificant. In our cases no differential study from this point of view is possible because in all instances both the cortex and the medulla have been markedly involved. In case 1 the origin of the tumour was of course from the medulla, but by simple increase of size the cortical part has been extensively involved by pressure effects. It is significant that in unilateral lesions there was no compensatory hypertrophy of the other healthy gland.

#### Summary

(1) In two thousand unselected autopsies, suprarenal lesions were found in sixteen cases.

(2) Out of three hundred and fifty-two cases of tuberculosis, pulmonary and intestinal, only two cases showed involvement of the suprarenal glands.

(3) A unilateral suprarenal lesion fails to produce Addison's syndrome and extensive bilateral destruction of the glands does not necessarily result in a frank picture of Addison's disease.

(4) Two cases of tuberculosis, a case of secondary actinomycosis, hæmorrhage, degeneration, secondary adenocarcinoma and ganglion neuroma of the suprarenal gland are described in detail.

Our thanks are due to Lieut.-Colonel J. C. De, Principal and Superintendent, Medical College, Calcutta, for the case records and also to the staff of this department specially to Dr. D. M. Gupta, M.B., Curator of the Museum, for the help rendered.

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## RESPIRATORY DYSPNOEA FOLLOWING ADMINISTRATION OF BARIUM MEAL

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THE purpose of this note is to bring to the notice of the profession that certain untoward symptoms may follow the administration of a barium meal. The senior author, as a visiting physician of the Carmichael Hospital for Tropical Diseases, Calcutta, has under his care a large number of cases of gastro-intestinal disorder and various other conditions where a search for septic foci is of primary importance from the point of view of diagnosis and treatment. During a patient's stay in the hospital a complete investigation is carried out as a routine procedure, and complete examinations of the blood, stools, urine, sputum, etc., are made. The administration of a barium meal to ascertain the condition of the gastro-intestinal tract has often to be done. In a previous paper Chopra, Hayter and Bhattacharya (1937) have given an account of the radiological investigations of the gastro-intestinal disturbances encountered in the tropics. Though no untoward effects were observed by them in a large series of cases after an opaque meal, the question of occurrence of toxic symptoms cannot be discarded altogether. Recently the present authors have observed marked symptoms of respiratory dyspnoea in two of their cases in the hospital, which apparently started after the administration of an opaque meal. One of these patients was admitted into the hospital with a history of asthma and had been under treatment for a long time for this condition. The other case gave no history of asthma at any period and was admitted for chronic gastro-intestinal disorder attended with pain in the right iliac fossa. The opaque meal was administered as follows:—

The patient was given 2 drachms of pulv. glycyrrhiza compound overnight followed by a simple enema the next morning. The contents of one vial of *citobaryum* (150 gm.) dissolved in about 16 ounces of milk were given. Skiagrams were taken, immediately after the meal, 5 hours, 10 hours, 24 hours, 48 hours and if necessary after 72 hours. No purgative was given to the patient before the x-ray examinations were completed, i.e., in the majority of the cases after 48 hours, and in some after 72 hours.

**Case 1.**—A Hindu female, aged 28 years, was admitted on 14th October, 1938, with history of asthmatic attacks, headache, irregularity of menstruation and leucorrhœa. She is the mother of eight children. There is no history of asthma on the father's side but the mother suffered from asthma.

Onset of asthmatic symptoms occurred soon after her marriage at the age of 15, after a 'cold' which

developed into chronic bronchitis; frequent attacks of asthma followed later. Severe attacks of asthma occurred after the birth of the first child; for these she received 30 injections of soamin and was free from symptoms for about two years. Curetting of the uterus was done after the birth of the second child and she was comparatively free from attacks till after the birth of the fourth child. From this time onward there was definite aggravation of the trouble and frequent attacks of asthma occurred. Change of climate did no good. A few months before admission into the hospital, the patient was experiencing difficulty in breathing throughout the greater part of the day and night and this could only be relieved with frequent injections of adrenalin. The asthmatic attacks were worse during the menstrual periods and during winter than during the summer. Heavy meals and rich food brought about an attack immediately; the patient was a strict vegetarian.

**Physical.**—She is fairly well built; tongue slightly coated; no evidence of sepsis in the teeth. There is some deviation of the septum to the right, and a certain amount of catarrhal ethmoiditis and generalized pharyngitis is present. The skin is normal at present but there is history of an urticarial rash two months previously. The lungs show prolonged expiration with marked wheezing sounds. The heart sounds are not strong but there is no abnormality. The liver and spleen are not palpable, there is tenderness and rigidity over the right iliac fossa. Tendon reflexes normal, the pupils react to light and accommodation normally.

**Laboratory investigation.**—Blood—hæmoglobin 108 per cent (Hellige), erythrocytes 5,520,000, leucocytes 7,900, polymorphonuclears 54 per cent, small mononuclears 37 per cent, large mononuclears 3 per cent, eosinophiles 6 per cent, Arneth count 40, 36, 16, 6.2, index 84. Stools contain no abnormal protozoa, bacteria or ova. There was nothing abnormal in the urine; blood pressure 110/90; gastric analysis showed normal acid curve; electrocardiogram normal. Skiagram of chest showed nothing abnormal except accentuation of the shadows of the bronchioles. Dermal tests for hypersensitiveness to foods were carried out with negative results. Sputum culture showed *Streptococcus non-hæmolyticus*, *Pneumococcus*, *N. catarrhalis*; no acid-fast bacilli found.

**P. V. examination.**—Uterus slightly retroverted. Cervix is healthy and there is no tenderness in the adnexa.

For purposes of investigation of the condition of the gastro-intestinal tract, barium meal was given on 10th November, 1938, and skiagrams were taken at the hours specified above. The reading of the x-ray plates showed:—

**Stomach.**—J-shaped; position and size normal; filling normal, motility and tone good, no ulcer. There was residue of meal after five hours which persisted for ten hours.

**Duodenum.**—Duodenal cap was well formed and there was no tenderness.

**After 10 hours.**—Jejunum and ileum showed residue at ten hours. Appendix visualized at ten hours.

**24 hours and 48 hours.**—The distal parts of the colon were spastic and showed the 'string sign' of colitis. The appendix was visualized, it was elongated, had irregular lumen and showed the presence of concretions. Residue in the appendix was visible after 48 hours, the tip appeared to be adherent and tenderness was present, probably pathological.

This patient with usual treatment for asthma was progressing satisfactorily. After the administration of a barium meal on 10th November, 1938, the patient had slight dyspnoea the same day which was controlled at first with anti-spasmodic drugs. Twelve hours after the meal the symptoms were considerably aggravated and the patient had very severe and persistent asthmatic attacks and developed well-marked

yanosis. Drugs such as ephedrine, atropine and even adrenalin which usually gave immediate relief failed to control the symptoms. She had severe dyspnoea all the time, so much so that oxygen had to be given with a nasal catheter continually for 24 hours. In addition, she was given glucose and sodium bicarbonate per rectum by the drop method. An attack of such severity and persistence has occurred for the first time. It lasted for nearly 72 hours and gradually subsided after the barium meal was thoroughly evacuated with purgatives.

**Case 2.**—E. M., male, aged 27 years, admitted with the history of an acute attack of pain over the right iliac fossa one year ago. A similar attack followed one month later, and subsequently the patient complained of localized tenderness over the region of the appendix, he was admitted for investigation on 22nd October, 1938.

**Physical examination.**—The patient was of average build. There was no evidence of sepsis in the teeth; tongue, ear, nose and throat showed no gross abnormality; lungs and heart normal; liver and spleen not palpable, genito-urinary tract nothing abnormal; the pupils reacted normally to light and accommodation; other reflexes normal.

**Laboratory examinations** showed stool negative to abnormal bacteria, protozoa and ova; urine no albumin, no sugar. Blood—haemoglobin 119 per cent (Hellige), erythrocytes 5,250,000, leucocytes 11,100, polymorphonuclears 54 per cent, small mononuclear 16 per cent, large mononuclear 10 per cent, eosinophiles 18 per cent, Arnett count 50, 30, 16, 3, 1, index 88. Blood pressure 120/80; gastric analysis showed a normal acid curve; dermal tests for hypersensitiveness to foods, negative; sputum on culture shows *Streptococcus non-haemolyticus*, *Pneumococcus*, and *N. catarrhalis*.

The patient was given a barium meal for examination of the appendix. On the day of examination he complained of an irritative cough which was relieved by administration of mild antispasmodics. Within twelve hours, however, he showed marked symptoms of dyspnoea with feeling of tightness across the chest which developed into a typical asthmatic attack. On examination of the lungs, inspiratory and expiratory rhonchi were heard all over on both sides. Skiagram of the chest revealed accentuation of the hilus shadow; peribronchial glands were calcified; no infiltration present. In the nose there was no gross abnormality but there was evidence of rhinitis.

The attack was persistent and the patient was given injections of adrenalin which gave him temporary relief. The acute symptoms lasted for about 48 hours and did not disappear till the barium meal was cleared with a purgative. The lungs did not clear up completely for about a fortnight.

The reading of the x-ray plates showed:—

Stomach normal size; motility normal.

4 hours. Stomach clear; meal rushed through the small intestines and reached the pelvic colon.

9 hours. The appendix was visualized and was coiled on itself.

24 to 36 hours. Residue was seen in the appendix. The appendix appeared to be pathological.

### Discussion

Two instances are recorded where, following the administration of a barium meal for investigation of the condition of the gastro-intestinal tract, the patients exhibited signs and symptoms similar to those of a severe attack of asthma. In case 1 the patient was a sufferer from asthma but in the other case, the patient was

admitted for pain in the iliac fossa and did not give any history of asthmatic attacks previously. Although these cases do not warrant a general conclusion to be drawn, the symptoms which followed were so striking that the subject is worthy of further investigation. In case 1, the symptoms occurred during the quiescent period when the patient had recovered with rest and treatment. The administration of a barium meal in this case appears to have brought about the attack in a very aggravated form. In the second case there was no history of asthma previously. The symptoms in very acute form appeared and severe dyspnoea lasting for about forty-eight hours followed. There was further a tendency to dyspnoea for about a fortnight after the administration of the meal.

What was the reason for the appearance of these asthmatic attacks? Were they due to some form of allergy or were they produced by the specific action of barium on the bronchial musculature. It is well known that barium is the most toxic of the alkaline earths. The soluble salts of barium are, however, absorbed very slowly from the intestinal tract. Barium sulphate, which is used for radiographic examination of the gastro-intestinal tract, is not absorbed, at least in any appreciable quantities, and passes through the body unchanged. It is, therefore, imperative that barium sulphate administered must be absolutely pure. Toxic symptoms have followed the administration of barium meals on account of contamination with more soluble salts such as the chloride or sulphide.

Further, barium has a specific action on both striped and the non-striped muscle. It has been shown that a more prolonged and stronger contraction may be obtained in a frog's muscle under its action, probably because of its stimulant action on the contractile substance of the muscle fibres. The contractions of the involuntary muscles in the body such as those of the gastro-intestinal canal, the bronchi, etc., are stimulated. Intravenous injection of barium salts in experimental animals produces augmentation of the movements of the involuntary muscles of the whole body with severe vomiting, evacuation of the bowels and the bladder and marked contraction of the bronchioles. This action of barium is thus a selective action on the smooth muscle.

It is, therefore, possible that minute quantities of barium may have been absorbed in these cases, producing contraction of the bronchial musculature and persistent symptoms of asthma. If that is so the quantities absorbed must be so minute as to be undetectable by the ordinary chemical or spectroscopic methods.

A further point of interest in both these cases is that the appendix was pathological and undoubted signs of irritability of the vagus were present. Whether the presence of this irritability rendered the musculature supplied by the

(Continued at foot of next page)

## NOTES ON THE KALA-AZAR RESEARCH IN CHINA

### THE USE OF 'DISTIBINYL' IN THE TREATMENT OF CHINESE KALA-AZAR

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#### I. Introduction

VARIOUS pentavalent antimony compounds, such as 'Neostibosan', 'Neostam', 'Aminostiburea' and 'Solu-stibosan', have been employed by workers in China, in India and elsewhere in the treatment of kala-azar. The only serious disadvantage of the pentavalent compounds is their high cost, a matter of some moment, when, as in case of China, some hundreds of thousands of kala-azar patients still require treatment. Attempt was made by Dr. C. K. Liang of the Department of Chemistry and Pharmaceutics, Central Field Health Station, Nanking, China, to obtain some form of pentavalent antimony compounds, if not better, at least equal to the various preparations which have already appeared in the market. A series of confirmed kala-azar cases has been put on trial by the author at the Kala-azar Research Station, Tsingkiangpu, the endemic centre of kala-azar in China in the year 1937, to see the efficacy of treatment with the native product which has been produced by Dr. Liang.

#### II. Chemical constituents and toxicity

'Distibinyl' is the diethylamine salt of di-*p*-aminophenylstibinic acid and contains 40.6 per cent of antimony. It is a greyish-white powder very soluble in water giving a brown-yellow solution. It is preserved in dry sealed tubes and is not stable if exposed to air for more than one day.

The toxicity of 'Distibinyl' has been tested on white rats. The maximum tolerable dose has been found to be 200 milligrammes per kilogramme of body-weight of rat.

#### III. Preparation of solution and mode of administration

'Distibinyl' is used intravenously dissolved in cold distilled water. The solution should not be boiled. For making solutions dissolve 0.05 gramme in 1 c.cm., 0.1 gramme in 2 c.cm., 0.2 gramme in 4 c.cm., 0.3 gramme in 6 c.cm., of water. Always use fresh solution.

(Continued from previous page)

vagus more sensitive to minute quantities of barium is a suggestion for consideration.

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Chopra, R. N., Hayter, R. T. M., and Bhattacharya, S. N. (1937). *Indian Med. Gaz.*, Vol. LXXII, p. 129.

#### IV. Method of study

Prior to the treatment, diagnosis was confirmed by the finding of *Leishmania donovani* from the liver puncture, either in direct smears or in culture. Patients were then admitted to the wards of the Kala-azar Research Station during the course of treatment under our close observation. Temperature, pulse and respiration were taken every day at 8 a.m., and 12, 4, and 8 p.m. Serum tests were examined before treatment, at cessation of treatment, and one month, three months and six months after treatment. Leucocyte and differential counts were taken regularly. Stool and urine samples were examined at different intervals to eliminate the other parasitic infections and to see if there was any albumin in the urine. Unfortunately our experiments had to be discontinued in the middle of November 1937 and the number of cases under our observation was limited to 126, out of which 55 cases came back three months and 14 cases came back six months after treatment. However, from the data obtained so far, we have concluded this experiment to see the efficacy of treatment with 'Distibinyl' and further study will be continued as soon as we resume our routine work in the Station at Tsingkiangpu.

The tables given are summarized results to date.

#### V. Dosage

The initial dose varies from 0.025 to 0.50 gramme with an average of 0.10 gramme. The maximum dose varies from 0.10 to 0.60 gramme with an average of 0.30 gramme. Number of injections varies from 6 to 14 with an average of 9. Number of days of injections during each course of treatment varies from 6 to 32 with an average of 10. For those cases treated for more than 15 days, the injections were duly given every other day instead of every day (tables III, IV, VI and VII). The total doses per 45 kilogrammes body-weight vary from 1.15 to 2.99 grammes with an average of 2.10 grammes to cure (table V).

#### VI. The course of disease under treatment

*The fever.*—After about the fourth injection the patient is usually free from fever. In the majority of cases, the fever disappears after the first or second injection, although in others a low fever persists until the week end after the beginning of treatment. A reactionary rise of temperature may occur after each injection, though a sudden sharp rise in a patient who has not previously shown any reaction is indicative of too large a dose having been given (table VIII).

*Body-weight.*—At the end of treatment, over 40 per cent of cases showed increased body-weight; the others with no increase and a few cases with slight decrease. At one month and three months after treatment there is a marked increase in all cases (table IX).

*Spleen and liver.*—In the majority of cases, the spleen decreases rapidly in size by the end of treatment. In some cases the decrease is slower, but decrease continues for some time after treatment has terminated. Practically the spleen becomes not palpable by the end of six months after treatment. The liver on the other

TABLE I  
*Age*

Age	Number of cases	Percentage
1-10	11	8.73
11-20	58	46.03
21-30	25	19.84
31-40	13	10.32
41-50	8	6.35
51-60	9	7.14
61-70	2	1.59
TOTAL	126	100.00

TABLE II  
*Sex*

Sex	Number of cases	Percentage
Male	92	73.02
Female	34	26.98
TOTAL	126	100.00

TABLE III  
*Initial dose*

Dosage	Number of cases	Percentage
0.025	6	4.76
0.05	39	30.95
0.10	53	42.07
0.15	26	20.63
0.25	2	1.59
TOTAL	126	100.00

TABLE IV  
*Maximum dose*

Dosage	Number of cases	Percentage
0.10	2	1.59
0.15	14	11.11
0.20	13	10.30
0.25	37	29.37
0.30	16	12.70
0.35	17	13.49
0.40	19	15.08
0.45	7	5.56
0.60	1	0.80
TOTAL	126	100.00

TABLE V  
*Total dose per 45 kilogrammes body-weight*

Dosage	Number of cases	Percentage
0.80-0.99	7	5.56
1.00-1.19	17	13.49
1.20-1.39	15	11.90
1.40-1.59	13	10.32
1.60-1.79	5	3.97
1.80-1.99	9	7.14
2.00-2.19	13	10.32
2.20-2.39	11	8.73
2.40-2.59	18	14.28
2.60-2.79	14	11.11
2.80-2.99	2	1.59
Above 3.00	2	1.59
TOTAL	126	100.00

TABLE VI  
*Number of injections*

Number of injections	Number of cases	Percentage
6	11	8.73
7	29	23.02
8	19	15.07
9	21	16.67
10	22	17.46
11	15	11.90
12	3	2.38
13	..	..
14	6	4.77
TOTAL	126	100.00

Average number of injections—9

TABLE VII  
*Days of injections*

Number of days	Number of cases	Percentage
6	11	8.73
7	29	23.02
8	19	15.08
9	23	18.25
10	14	11.11
11	11	8.73
12	4	3.17
13	1	0.79
14	5	3.95
15	1	0.79
20	1	0.79
21	1	0.79
23	1	0.79
26	3	2.33
30	1	0.79
32	1	0.79
Total	126	100.00
Average	10	..

hand rarely decreases until after the injections have been discontinued (tables X and XI).

*General condition.*—The general condition improves almost immediately, the improvement being noticeable even after one or two injections.

*Length of the course of treatment.*—The length of the course of treatment at present is difficult to determine. The mean total dose per

45 kilogrammes body-weight was 2.1 grammes with an average number of ten injections.

*Laboratory findings.*—Over 56 per cent of the cases showed negative findings for *Leishmania donovani* from their liver punctures at the end of treatment. Practically all the cases became negative one month after cessation of treatment (table XII).

The increase of white cell counts, increase of polymorphonuclears, decrease of large mononuclears and marked increase of eosinophiles are also indications of cure (tables XIII and XIV).

The result of the sero-reactions on the cases resembles that obtained from those cases treated with other antimony preparations, i.e., the peptonate of iron test also acts as the 'signal' for cure and it becomes negative in all cases about six months after treatment.

#### VI. Complications associated with treatment

Some complications of kala-azar which sometimes arise during treatment with other antimony preparations, namely, pneumonia, shock, urticaria, ascites, jaundice, hæmoptysis, herpes zoster, mastoiditis and nephritis, have not been observed in any of our cases. Slight degree of diarrhoea and vomiting is not infrequently encountered when too large a dose has been given. Slight abdominal pain was observed in 50 cases whose stool examinations all revealed numerous ascaris eggs. Epigastric distress, cough and headache were present in 12, 15 and 9 cases respectively. One case each showed swelling of scrotum and blister formation and similar conditions have also been observed in the treatment with other antimony preparations.

TABLE VIII  
*Subsidence of fever*

After the beginning of treatment	Number of cases	Percentage
Total	126	100.00
1 day	80	63.49
2 days	20	15.87
3 "	14	11.11
4 "	5	3.97
5 "	3	2.38
6 "	1	0.80
7 "	3	2.38

TABLE IX  
*Increase of body-weight*

	END		1 MONTH		3 MONTHS		6 MONTHS	
	No.	%	No.	%	No.	%	No.	%
No increase	31	56.36	7	12.73	2	3.51	..	..
Increase	24	43.64	48	87.27	55	96.49	14	100.00

TABLE X  
*Enlarged spleen*

	BEFORE TREATMENT		END OF TREATMENT		ONE MONTH AFTER TREATMENT		THREE MONTHS AFTER TREATMENT		SIX MONTHS AFTER TREATMENT	
	Num-ber	Per-centage	Num-ber	Per-centage	Num-ber	Per-centage	Num-ber	Per-centage	Num-ber	Per-centage
Enlarged spleen	126	100.00	13	10.32	..	..	..	..	..	..
Decrease in size	..	..	110	87.30	80	76.92	20	36.36	1	7.14
No change	..	..	3	2.38	24	23.08	35	63.64	13	92.86

TABLE XI  
*Enlarged liver*

	BEFORE TREATMENT		END OF TREATMENT		ONE MONTH AFTER TREATMENT		THREE MONTHS AFTER TREATMENT		SIX MONTHS AFTER TREATMENT	
	Num-ber	Per-centage	Num-ber	Per-centage	Num-ber	Per-centage	Num-ber	Per-centage	Num-ber	Per-centage
Total	126	100.00	126	100.00	104	100.00	55	100.00	14	100.00
Enlarged liver	126	100.00	49	38.89	19	18.27	3	5.46	..	..
Decrease in size	..	..	76	60.32	76	73.08	25	45.45	3	21.43
No change	..	..	1	0.79	9	8.65	27	49.09	11	78.57



PLATE XIII



Fig. 1a.



Fig. 1b.



Fig. 1c.



Fig. 2a.



Fig. 2b.



Fig. 2c.



Fig. 3a.



Fig. 3b.



Fig. 3c.

Showing progress in three typical cases:

(a) Before treatment.

(b) One month after treatment.

(c) Six months after treatment.

## CONGENITAL CYSTIC DISEASE OF THE LUNGS

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THIS condition has gone under a variety of names in the past, foetal bronchiectasis, congenital bronchiectasis, atelectatic bronchiectasis, and congenital pulmonary lymphangiectasis, but now it is generally known as congenital cystic disease of the lungs. Some standard works fail to mention it at all; others barely mention it, or refer to it as rare or as chiefly of interest to the pathologist. Still others mention its occurrence, but make little or no attempt to describe it. Boyd (1935) indicates its clinical importance and Norris and Landis (1933) give a fairly adequate description. All are agreed in calling the condition rare; more recent investigations would not seem to bear out this statement.

Until 1925, apparently no case was diagnosed clinically. In that year, Koontz (1925) reported 108 cases collected from the European literature and added one of his own. All had been diagnosed upon the autopsy findings. In 1936, Schenck (1936) collected an additional 124 cases from the world's literature and added four of his own. In the following 1½ years, Schenck (1937) reported that an additional 140 cases had

been described and to these he has added another five cases of his own, making a total of 381 cases reported since Bartholinus recorded the first case in 1687. The great majority of these cases have been reported in the last few years. Now that diagnosis has become possible during life, some of these cases have even been successfully treated.

There is no evidence that either syphilis or Koch's bacillus plays any part in the causation of this condition. The precise pathogenesis is unknown, but the prevailing opinion is that the lesion is a congenital anomaly or malformation caused by the pinching off of a small pulmonary bud during the development of the lung; this pinched-off bud continues to develop. The wall of the resulting cyst is made up of high or low columnar epithelium which may or may not be ciliated. Along with the epithelium there is muscle, elastic tissue and cartilage arranged sporadically. All point to the bronchial origin of the cyst. The retained secretions are apparently of mucosal origin. The absence of anthracotic pigment in the wall of the cyst or in its immediate vicinity would indicate its functionless nature. Other congenital anomalies of a pulmonary nature frequently are present in the same patient, often taking the form of accessory lobes or accessory lungs.

Reisner and Tehertkoff (1937) feel, however, that the cause is an arrested development of the lung with a failure of the pulmonary parenchyma to form, while the existing bronchial ramifications continue to grow into abnormally large spaces. As the lungs are inflated with air after birth these spaces are distended into cysts or air-sacs. According to this theory, large, solitary cysts result if the arrested development occurs early in intra-uterine life at the time when only the stem bronchus or the lobar branches are found. The smaller multiple cysts result when the arrested development occurs later. By still other writers, inflammatory processes during foetal life have been blamed.

The cysts are solitary or multiple. They contain a milky or turbid fluid at birth and this fluid will persist unless it is evacuated by rupture into a bronchus or bronchiole. When this occurs, air will replace the fluid. If the communication thus established between the cyst and the bronchus remains open and free so that air may pass in both directions, the cyst will remain stationary in size and non-expansile. Should air be able to enter the cyst, but not be free to leave because of some valve-like effect at the communication an expansile, balloon type of cyst is produced with severe clinical results. The same mechanism is found active in both solitary and multiple cysts. Any portion of the bronchial tree or of the interstitial pulmonary tissue may be involved in the production of these cyst formations. Sauerbruch (1934) believes that 80 per cent of bronchiectases seen in children and limited to one lobe are congenital in origin.

(Continued from previous page)

spleen and liver, increase of leucocyte counts, increase of polymorphonuclear neutrophile leucocytes and negative results of sero-reactions.

4. During the course of treatment and after cessation of treatment, rest and nutritious diet containing eggs and liver, will hasten the process of recovery.

5. Further study will be continued later on to see whether there is any relapse or re-infection among the treated cases.

### VIII. Acknowledgments

The writer wishes to express his gratitude to Dr. F. C. Yen, Director, and Dr. P. Z. King, Deputy Director, of National Health Administration, to Dr. J. Heng Liu, formerly Director, Central Field Health Station, N. E. C., China, and Dr. Y. T. Yao, Chief of the Department of Parasitology, for their constant interest and encouragement on this piece of work. The writer also has pleasure in thanking Dr. C. K. Liang, Chief of the Department of Chemistry and Pharmaceutics, Central Field Health Station, and his assistants for their painstaking work in the constant supply of such a drug for this study.

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Schenck (1937) has modified the classification of Anspach and Wolman (1933) as follows:—

- A. Solitary fluid cyst (at birth).
  1. With no bronchial communication—solitary fluid cyst.
  2. With bronchial communication—solitary air cyst.
    - (a) With free opening—non-expansile air cyst.
    - (b) With one-way mechanism at the orifice—expansile air cyst.
- B. Multiple fluid cysts (at birth).
  1. With no bronchial communication—multiple fluid cysts.
  2. With bronchial communication—multiple or trabeculated air cysts.
    - (a) With free opening—non-expansile trabeculated air cysts.
    - (b) With one-way valve mechanism at the orifice—expansile trabeculated air cysts.

The clinical manifestations of congenital cystic disease vary greatly and they depend chiefly on the extent of the lesions, their site and whether or not changes in the cysts cause changes in the intra-thoracic pressure. Symptoms of the condition are usually present from birth or make their appearance shortly thereafter. The usual clinical picture is that of recurring attacks of dyspnoea and cyanosis with or without cough. These attacks may be so mild as to escape notice or they may be so severe as to result in death. Eloesser (1931) claims that these attacks occur only when there exists an imperfect communication between the cyst or cysts and bronchus and that they should be absent either when the communication is free or does not exist at all. The attacks are most prominent when the communication is valve-like in nature and in such cases the attacks may not be relieved until the trapped air is removed by puncture, ruptures into the pleural sac, or manages to overcome the valve-like nature of the communication.

Expectoration occurs only if the cyst communicates with a bronchus, and only then if secondary infection has occurred. Such cases may be very suggestive of bronchiectasis. Haemoptysis may occur and be slight or well marked enough to suggest the presence of tuberculosis. Less frequent symptoms as weakness, anorexia, palpitation and emesis may occur. Referred epigastric pain is sometimes present. The dyspnoea and wheezy breathing are very suggestive of asthma.

Physical signs are seldom very definite. They vary with the number and with the contents of the cysts present. They usually are sufficient to indicate the presence of a pulmonary lesion but rarely will they indicate its nature. Progressive dyspnoea in an adult without any apparent cause and with or without a history of preceding inspiratory infection should suggest the possibility of the existence of the condition.

For diagnosis, Wood (1934) claims that a satisfactory roentgenological study is necessary. He also states that in many instances bronchoscopic examination or x-ray after the introduction of iodized oil intrabronchially or the induction of

a diagnostic pneumothorax may be further required. Such procedures are all within the realm of the modern diagnostic clinic. The differential diagnosis will depend upon the type of cyst that is present.

Fluid-containing cysts, especially if they are full so that no fluid level appears on the skiagram, must be differentiated from intra-thoracic tumours, pulmonary abscess, empyema and dermoid or echinococcus cysts. If no fluid level appears it is impossible to tell them from tumours except by exploratory thoracotomy (Wood). An infected cyst will simulate an abscess both clinically and roentgenologically and in such cases the use of the bronchoscope, of x-ray after iodized oil, or the observance of the subsequent course of the disease may be necessary in order adequately to distinguish them. The shadow cast by the fluid-containing cyst is circular or rectangular whereas that cast by an empyema is more triangular and has its base at the thoracic wall. Echinococcus cysts will give a positive complement-fixation reaction and clinically there is urticaria and eosinophilia. Such cysts are mediastinal in origin and cause little or no dyspnoea. The characteristic hooklets may be found in the sputum. Unless teeth, bone or cartilage appear on the x-ray film, it may be impossible to distinguish a dermoid cyst.

If the cysts are air-containing, the differential diagnosis becomes still another problem. The physical examination is of little or no use. In large balloon-type cysts both the physical examination and the skiagram may suggest a pneumothorax. The skiagram in pneumothorax, however, will show the well-defined border of the collapsed lung which is not seen in the film of a cyst. If the cyst communicates with a bronchus iodized oil should outline its borders, or, if it does not, an induced pneumothorax followed by x-ray will usually distinguish it. An infected honey-comb lung will closely simulate bronchiectasis, but here bronchoscopy and iodized-oil instillation followed by x-ray will usually readily differentiate the two conditions.

Not infrequently the x-ray will show an extensive lesion when the patient appears to be quite comfortable and with surprisingly few symptoms. Schenck feels that this is an important point to remember in the differential diagnosis.

The inflammatory lesions usually offer less difficulty, particularly if they are acute or sub-acute in nature. Pneumonia offers no problem at all. An encapsulated empyema will have a history of a recent acute infection and a septic fever. The x-ray will show a localized pocket of fluid. If this is interlobar, the shadow will be wedge-shaped and will extend along the situation of the interlobar fissure. Lung abscesses can usually be diagnosed by their previous history, their course, and the poorly-defined margins of the lesion on x-ray, because of the surrounding pneumonitis.

The solitary non-expansile cyst appears as an inter-pulmonary globular or spherical pocket of

air that often shows increased illumination on deep inspiration under the fluoroscope. It must be differentiated from an emphysematous bulla which would have no delimiting wall, from a localized or partial pneumothorax which would be outside the lung parenchyma, would be more irregular in contour and would show no increased illumination on deep inspiration, and from a tuberculous cavity which would show dense broader walls, concomitant pulmonary infiltration and other changes that accompany this disease. Nevertheless many cases of solitary cysts have received anti-tuberculosis treatment by mistake.

The expansile or balloon-type cyst causes increasing symptoms of dyspnoea and cyanosis. The x-ray picture may closely simulate that of a complete pneumothorax and differentiation may be quite difficult. There may be some haziness at the apex and obliteration of the costo-phrenic angle because of atelectasis. The hilar shadow may be narrow and elongated, and there may be a broad stump at the lung root as in pneumothorax. It may be necessary to induce pneumothorax so that the outer border of the lung and the wall of the cyst might be refracted from off the chest wall and then to x-ray in order to separate the two conditions, diagnostically. The clinical picture in the two conditions may be approximately or identically the same.

Multiple air cysts show up in the skiagram as sharply-defined spherical cavities, discrete, irregularly arranged and with a lack of infiltration in the pulmonary tissue between them. Clinical signs may be few or none at all. Bronchiectasis may be confused with this condition, but this usually follows a severe infection and the skiagram will show secondary changes in the pulmonary tissue between the cavities. The cysts may give a history of more or less mild symptoms since birth.

The differentiation of diaphragmatic hernia and eventration of the diaphragm from these conditions is suggested by the absence of gurgling sounds, and is accomplished by the barium meal followed by x-ray examinations.

The prognosis in congenital cystic disease is, on the whole, not good. The condition is not compatible with long life and, according to Schenck (1937), the mortality is high among children, especially with the expansile type. The greatest potential danger is from secondary infection. If no bronchial communication exists, the patient is safer and the condition is less likely to progress.

The only rational treatment is surgical extirpation or lobectomy in selected cases. With improved technique the mortality rate from this procedure is decreasing and the operation is becoming more feasible. Wood (*loc. cit.*) claims that, in infected cases, bronchoscopic aspiration followed by the injection of iodized oil has produced marked subjective improvement. If the intra-thoracic pressure is increasing, repeated aspirations or the institution of per-

manent thoracic drainage may become necessary to save the patient's life. Aspiration will confer no benefit unless there is this increasing pressure. At times symptoms may subside spontaneously, presumably either because the cysto-bronchial communication has become blocked completely or has become quite free, the valve-like action in either case being abolished.

*Case report.*—Male, aged 17, a schoolboy, was admitted to the wards of the Miraj Medical Centre on 10th November, 1938. He complained of dyspnoea which was more marked on exertion, and of a chronic cough which was accompanied by small amounts of sputum. As far as he knew, these symptoms had been present all his life and were worse during the rainy season. He had never had an attack suggestive of true asthma nor did he ever feel uncomfortable because of his symptoms. Two months prior to admission he had had a small hæmoptysis and, because of this, a diagnosis of tuberculosis of the lungs had been made. He was referred to the Wanless Tuberculosis Sanatorium where the diagnosis could not be confirmed. He was therefore sent to the Miraj Medical Centre for further study.

His family history was essentially negative. Beyond admitting smallpox four years previously, the patient denied any preceding illness, including the usual ones of childhood. The boy was an orphan since early childhood, his parents having died of causes unknown. He had neither brothers nor sisters.

Physical examination revealed a well-developed and well-nourished boy of 17 lying quietly in bed and not obviously ill. He weighed 68 lb. The head was normal. The ears contained inspissated wax which was subsequently removed. The nose and throat were quite clear of anything pathological. The tonsils, teeth and gums were all healthy. The tongue was clean. The thyroid was not palpable. The anterior and posterior cervical glands were palpable and there was one large gland the size of the tip of the little finger in the centre of the right posterior triangle. Other smaller glands were palpable above the middle third of the right clavicle. The cardiac impulse was localized at the apex, which was situated in the fifth intercostal space, well within the left nipple line. The cardiac sounds were clear and forceful and the second pulmonic was accentuated. There were neither thrills nor murmurs. The thoracic cage was sthenic in type and moved freely on respiration. The lungs showed increased resonance throughout both sides, anteriorly and posteriorly. The breath sounds were harsh and the expiratory murmur was prolonged. There were many coarse and medium râles and rhonchi throughout both lungs. Vocal and tactile fremitus were both diminished. The abdomen, liver and spleen showed nothing remarkable. The neurological signs were also normal as well as the skin, locomotor system and the peripheral arteries. The temperature was 98°F. and did not vary during his stay in the hospital. The pulse rate was 80 and the respirations were 22.

Neither the urine nor stool showed anything abnormal. The blood picture was as follows:—

Red blood cells	..	..	4,110,000
Hæmoglobin	..	..	90 per cent.
White blood cells	..	..	14,000
Polymorphonuclears	..	..	63 per cent.
Lymphocytes	..	..	35 "
Monocytes	..	..	1 "
Eosinophils	..	..	1 "

The sputum was repeatedly negative for tubercle bacilli but it was thick and foul and contained many leucocytes. Old tuberculin, 0.1 mgm., intracutaneously, failed to give any reaction. The sedimentation rate of erythrocytes was 19 mm. in one hour, the Cutler method being used (normal rate 0-10 mm.).

The x-ray (figure 1) showed many annular shadows scattered through the middle and lower areas of both lungs. These were close to the hila above but farther

out below. In the left hilar region one showed a fluid level and the suggestion of inflammatory thickening of the walls. There was a row of blebs down the left



Fig. 1.

border of the cardiac shadow. After intratracheal instillation of iodized oil into the left base (figure 2),



Fig. 2.

the outlines of the cysts became even more apparent. These pictures were considered as typical of congenital cystic disease of the lung.

Because of the mildness of the symptoms, no treatment beyond postural drainage and attention to the general nutrition was recommended, and the patient was discharged to one of the out-dispensaries for further observation and follow-up.

(Continued at foot of next column)

## UTERINE RETROVERSION

A COMMENTARY ON THE INDICATIONS FOR THE OPERATIVE CORRECTION OF RETROVERSION OF THE UTERUS, UNACCOMPANIED BY PROLAPSE—ILLUSTRATED BY SIX CASES

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It is well known that retroversion of the uterus can be present without causing any symptoms or signs by its abnormal position.

Theilhaber (1885) was the first to state that uncomplicated displacement of the uterus need cause no symptoms. Others—amongst them Curtis, C. Jeff Miller, Lynch and Crossen, quoted by A. H. Curtis (1933)—hold that retroversion, if long continued, will cause pathological changes in the pelvis. This will give rise to definite signs and symptoms which are characteristic of the condition.

The woman in whom the retroversion is due to hypoplasia of the uterus rarely has symptoms due to the retroversion.

The woman in whom the retroversion is directly attributable to childbirth will generally have symptoms due to the retroversion. The symptoms tend to be slow in onset and gradual in development.

Thirdly, there is the woman with a retroversion accompanied by other pathological conditions present in the pelvis—inflammatory or neoplastic. This woman will have symptoms chiefly referable to the associated conditions and only partly to the presence of the retroversion.

Examinations have shown that—

(a) 20 per cent of women have the uterus directed backwards without having had any

(Continued from previous column)

### Summary

The literature on congenital cystic disease of the lung is reviewed, and a case is reported.

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symptoms attributable to the displacement, as stated by Kerr, Ferguson, Young and Henry (1933).

(b) many women who complain of certain symptoms commonly associated with gynaecological conditions and who are found on examination to have the uterus directed backwards, when the position is corrected this group of patients still complains of their original symptoms.

In spite of the uterus being retroverted, we frequently see many women who, besides not complaining of any symptoms, carry out normally the functions of their pelvic organs. Thus menstruation may be normal in periodicity, amount, and duration, with very little menstrual pain. Pregnancy can, and often does, occur in the retroverted uterus and proceeds normally to term.

Anatomically, the uterus may be simply retroverted in position and all the other internal genital organs are normal in position and appearance.

Commonly, however, especially in the acquired variety of retroversion, the ovaries show some degree of prolapse into the pouch of Douglas. This may cause the broad ligaments to become folded over the utero-sacral ligaments, and in consequence results in pressure being exerted on the walls of the ovarian veins and veins of the pampiniform plexus, Clare (1933). Thus a broad ligament varix may result which exerts an influence on the function of menstruation and ovulation, and in addition is capable of causing persistent dull pelvic pain which may make a patient feel ill, particularly after being on the feet for a long time.

Graafian follicles under these conditions tend to be œdematous and persistent, and the uterine endometrium to be congested and thickened, Eden and Lockyer (1935).

Ovulation is irregular and this influences the endometrium with the result that irregular and profuse uterine bleeding may occur.

The other common anatomical modification with retroversion is uterine descent, but this does not concern us here and will not be discussed further.

In a great number of cases the following main symptoms, in greater or lesser degree, are present :—

- (1) Pain in the lower abdomen and back.
- (2) Menorrhagia, metrostaxis, menorrhagia, and leucorrhœa.
- (3) Dyspareunia.
- (4) Sterility.

There is no symptom-complex which is diagnostic of the condition of retroversion of the uterus. The symptoms already given may correctly fit any other gynaecological condition.

1. *Pain*.—This is usually of a dull, aching character and is usually most marked when the ovaries are prolapsed. It may occur as a dragging sensation in one or both iliac regions.

Backache is common. It is lumbo-sacral in position. Naturally, backache is not distinctive of retroversion. Its causes are many, but Lynch (1926) found backache in 50 per cent of patients with retroverted uterus and was able to relieve it in 81 per cent by suspension operations. Bullard (1921) reported that in 103 out of 129 cases, i.e., 80 per cent, backache was relieved by suspension operations for uncomplicated retroversion of the uterus.

Graves (1923), in an analysis of 500 cases of retroversion from all causes, states that lumbo-sacral backache was a definite symptom in 76 per cent.

Sturmdorf (1931) states that, in his opinion, the displacement is not the cause of the backache. He argues that the cause of the displacement is the cause of the backache. This hardly agrees with Bullard's findings or with those of Lynch (*loc. cit.*). Their results argue a possible indication for operative treatment.

The backache is said to be caused by traction on the utero-sacral ligaments. It is aggravated by prolonged activity and by menstruation, but is relieved by rest.

2. *Menorrhagia, metrostaxis, menorrhagia, and leucorrhœa*.—These are common symptoms and are due to the altered state of the endometrium. Owing to the œdema and persistence of Graafian follicles, reputed to be due to a prolapse of the ovaries, the endometrial condition has some points of resemblance to that of metropathia hæmorrhagica and therefore is capable of producing similar symptoms.

The symptoms of irregularities of the hæmorrhagic loss can occur in the absence of ovarian prolapse. If due to the retroversion they may be explained by the general congestion of the pelvic organs, secondary to the retroversion.

3. *Menstrual pain*.—This may be due to :—

(a) Congestion.

(b) Mechanical difficulty which the uterus encounters in expelling the menstrual products.

It must be realized that a uterus fully retroverted has its fundus at a lower level than the os internum. It therefore follows that the menstrual products have to be expelled against the force of gravity. For this reason the uterine muscle is called upon to perform extra work, and, as it is often on the borderline of muscular inefficiency, muscle spasm occurs producing severe menstrual pain.

4. *Dyspareunia*.—This is usually caused by prolapse of the ovaries. When the latter are in the pouch of Douglas, they are congested owing to their abnormal position, and in consequence are excessively tender to the touch. The usual sensitiveness is accentuated.

Dyspareunia can occur, apart from prolapse of the ovaries. The fundus of the uterus itself can be very tender especially when fixed in the pouch of Douglas by adhesions. For this reason, coitus becomes to all intents and purposes impossible, and marital unhappiness is likely to ensue.



5. *Sterility*.—As has been stated before, retroversion is by no means an absolute cause of sterility, but it has often been observed that after several years of sterile marriage, the correction of the retroversion of the uterus has been followed by pregnancy.

Sharman (1932) found that in his series of cases, 25 per cent were sterile.

Theoretically, sterility connected with uncomplicated retroversion of the uterus may be due to :—

(i) Alterations in the endometrial constitution which renders it an unsuitable nidus for implantation.

(ii) Coitus in the dorsal position deposits semen in the posterior vaginal fornix, towards which the normally situated cervix points. In retroversion the cervix points forwards, away from the posterior fornix and is often applied directly to the anterior vaginal wall. The spermatozoa therefore find it difficult to reach, and entry into the cervical canal is therefore not likely.

Hulmer thinks that only those spermatozoa directly ejaculated into the canal stand a reasonable chance of fertilizing an ovum, although others like van der Velde do not believe this to be true.

When correction of the retroversion has been decided upon, two technical procedures are available :

(1) The operative method, designed to maintain the uterus permanently in a position of anteversion.

(2) The instrumental method in which the uterus is kept anteverted by means of a mechanical support or pessary in the vagina.

The use of (2) is limited. It can be used with advantage in—

(a) puerperal backward displacement. It is possible to cure permanently a retroversion of this type if the pessary be left *in situ* for 2 to 3 months;

(b) those cases in which it is used as a diagnostic aid;

(c) patients not desirous of undergoing operative treatment.

Those cases grouped under (a) and (c) above do not concern us in this commentary, but those under (b) are important as this is the group in which operation is most likely to be indicated.

One may conclude that the signs and symptoms which are indicative of operative treatment come under the following headings :—

1. Those cases where the symptoms disappear when a pessary is used, indicating that symptoms are directly referable to the retroversion. Therefore, if an anteverting operation be properly and carefully carried out, it can be confidently expected that the symptoms will be cured. In this type of case the pessary is used as a diagnostic measure.

The only exception to this procedure is the sterile woman who has become pregnant after

the uterus has been kept anteverted by means of a pessary. Here, if the uterus be kept in an anteverted position during the ensuing puerperium, it may remain anteverted.

2. Those signs which cannot be treated by means of a pessary. These include dyspareunia due to either—

(i) prolapsed ovaries,

(ii) fixed retroversion.

Laxity of the vagina is an additional indication for operative correction.

A pessary stays with difficulty in a lax vagina, or it frequently turns sideways and renders no useful service.

3. Those cases in which the pessary fails to keep the uterus in the anteverted position.

It will be seen that the use of the pessary is a very valuable means of helping us to arrive at the decision of 'operation' or 'no operation'.

Unfortunately, in India it is a form of diagnosis and treatment which cannot be used to any extent for the following reasons :—

A. People (especially the hospital class—mostly coolies) move frequently from place to place. They attend hospital on one occasion and when asked to return in a week, they can rarely be induced to carry out the instruction.

B. If the pessary cures their symptoms, they are quite content never to appear at the hospital again.

It therefore follows that the pessary once having been introduced into such patients, never sees daylight again. The probable result is ulceration of the vagina with its common sequelæ, namely, carcinoma and general pelvic infection, which are common enough in India. Under these conditions the pessary becomes a potentially dangerous instrument and rarely can be used.

In the illustrative cases accompanying this article, the main symptoms for which operation was performed were sterility and dyspareunia.

This agrees with the reply to the inquiry sent to the senior gynaecologists at the London teaching schools, as mentioned by Luker (1934) in his article. Both these conditions, if present, play a large part in the life of the average woman, especially in India. For this reason, operative treatment—with us, Gilliam's technique—is performed as a routine if a woman complains of sterility and has a retroverted uterus.

Also, in the case of dyspareunia, operation is decided upon if the uterus be retroverted and tender on palpation, either with or without prolapsed ovaries.

All six cases are illustrative of this rule as applied to sterility.

Cases I, III, and VI are illustrative of sterility combined with dyspareunia which constitutes a double indication for operation.

In summary, the general indications for operation in this condition are much the same as those recorded by Luker (*loc. cit.*) with certain special

provisions dependent on the peculiar characteristics of the Indian mind, climate and other conditions of an economic nature.

It is regretted that no 'follow-up' report of these cases can be included.

Most of these people can be persuaded to come into hospital only when so driven by pain and disease. Very rarely can they be induced to attend for examination when feeling well.

One hopes that, in their failure to report, it may be surmised that the operation has relieved them of their symptoms.

I wish to thank Major-General N. M. Wilson, C.I.E., O.B.E., K.H.S., I.M.S., Surgeon-General with the Government of Madras, for permission to publish this commentary.

*Case I.*—Age 33 years; race Hindu; married 17 years; number of children 1, forceps delivery; number of abortions 1; last child—16 years ago; last abortion—14 years ago.

Admitted 26th July, 1937.

*Present history.*—Complains of pain in the back and lower abdomen for the last one year. Used to have pain on and off before this since the abortion fourteen years ago, but only occasionally. Pain has no relation to periods and the ache in the back is constant. Has no relation to food. Has no pain elsewhere in the body. No dyspareunia. No frequency of micturition or dysuria. No constipation.

*Periods.*—Regular. 30/3 days. They have become more scanty during the last few months. Sometimes has dysmenorrhœa before the period. Ceases with the flow. No leucorrhœa.

*Examination.*—Heart, lungs and abdomen. Nil abnormal.

*Vaginal examination.*—Cervix pointing downwards and forwards. Uterus retroverted. Normal in size. Ovaries palpable at the postero-lateral angles. Normal in size.

*Urine.*—1020 acid. Nil abnormal.

*Hb.* 75 per cent. *R. B. C.* 4.8 million. *W. B. C.* 7200. *B. P.* 110/75.

30th July, 1937. Under spinal anæsthesia laparotomy performed. Abdomen opened through mid-line sub-umbilical incision. Uterus found normal in size and shape but retroverted. Both ovaries large and fibrotic—dense white in colour. Tubes healthy. Both patent. Appendix long and bound down by adhesions to the cæcum. It was kinked and swollen at the end. Appendicectomy performed and Gilliam's suspension carried out. Abdomen closed. The patient made an uninterrupted recovery.

*Remarks.*—This was a case of sterility of sixteen years' duration after forceps delivery. On examination nothing abnormal could be made out to account for it, except a retroverted uterus. This sterility therefore was considered to be a definite indication for a suspension operation. Laparotomy was carried out and a Gilliam's operation done. The ovaries had a very thickened tunica albuginea and were fibrotic. This probably partly accounted for her sterility as her menstrual history indicated deficient ovarian function. The appendix showed signs of subacute and chronic inflammation and was removed. She made an uninterrupted recovery.

*Case II.*—Age 34 years; race European; married 11½ years; number of children 2, both normal confinements; number of abortions, nil; last child—7 years ago.

*Present history.*—Complains of backache for the last five years, which is becoming worse. She also has excessive loss at the periods. No lower abdominal pain. Has dyspareunia. No dysuria or frequency of micturition. Not constipated. No leucorrhœa.

*Periods.*—Regular. 28/5 days. Excessive loss with aching pain during period. Last period 12th January, 1938.

*Examination.*—Heart, lungs and abdomen. Nil abnormal.

*Vaginal examination.*—Cervix pointing downwards and forwards. Uterus retroverted. Fornices clear. Ovaries normal in size. Uterus is rather fixed and cannot be anteverted. Tender.

*Urine.*—1010 acid. Nil abnormal.

*Hb.* 85 per cent.

*B. P.* 110/70.

2nd February, 1938. Under spinal anæsthesia laparotomy performed. Abdomen opened through mid-line sub-umbilical incision. Uterus found retroverted and bound down by some thin adhesions. Rather red and congested. Tubes patent, and ovaries normal. Gilliam's suspension performed.

*Remarks.*—This was a case of sterility and dyspareunia. The patient was anxious to have another child and as she also had very painful coitus *plus* the fact that the uterus appeared fixed, a suspension operation was considered indicated. This was done by Gilliam's technique and the patient made an uninterrupted recovery.

*Case III.*—Age 19 years; race Indian Christian; married 4 years; number of children, nil; number of abortions—2 (1, 3rd month), (2, 2nd month); date of last abortion—8 months ago.

Admitted 18th March, 1938.

*Present history.*—Complains of pain in the lower abdomen and backache for the last eight months. Pain is definitely worse during the period. She had backache before her last abortion but this has definitely become worse since. No constipation, no pain on defæcation. No frequency or pain on micturition. Has dyspareunia.

*Periods.*—Regular. 28/8 days. Moderate loss. Last period 20 days ago. She has had leucorrhœa since marriage, which has become worse lately.

One year ago was admitted with dysmenorrhœa. Cervix dilated and curetted and the uterus anteverted manually, following the first abortion. She became pregnant but aborted four months after the operation.

*Examination.*—Heart, lungs and abdomen. Nil abnormal.

*Vaginal examination.*—Long conical cervix pointing downwards and forwards. Uterus retroverted, normal in size. Both ovaries prolapsed and tender. Fornices otherwise clear.

*Urine.*—Nil abnormal.

*Hb.* 55 per cent.

*B. P.* 115/80.

23rd March, 1938. Under spinal anæsthesia laparotomy performed. Abdomen opened through mid-line sub-umbilical incision. Uterus found retroverted, normal in size. Both ovaries prolapsed, tubes inflated and found patent. Uterus anteverted by Gilliam's technique, abdomen closed in layers.

26th March, 1938. Patient had reasonably comfortable night; passed urine and flatus: no vomiting, upper abdomen rather distended, to have enema.

13th April, 1938. Discharged fit.

The patient had unexplained pyrexia for about a week, but otherwise no complications and was discharged on 13th April.

*Remarks.*—A case of retroverted uterus, with prolapsed ovaries. The history and symptoms seem to point to the retroverted position of the uterus and prolapsed state of the ovaries being the cause of her trouble. There was a relative sterility (two abortions) which in the absence of any other cause was attributed to the retroverted uterus. The prolapsed ovaries were causing dyspareunia and as there seemed to be a better likelihood of her carrying a pregnancy to full term if the uterus were anteverted, the abdomen was opened and a Gilliam's operation was done. She made an uneventful recovery.

*Case IV.*—Age 29 years; race Hindu; married 12 years; number of children, nil; number of abortions, nil.

Admitted 19th July, 1937.

*Present history.*—Complains of pain in the lower abdomen. More on the right side. Has had it for

the last seven years on and off. No indigestion, has flatulence. Pain not related to taking of food. Starts about ten days before the period. Pain disappears when the flow starts. No vomiting, no backache. Tends to be constipated. No pain on defecation.

*Periods.*—Regular. 25/2 days. They are scanty, blackish in colour. Last period one week ago. She has no leucorrhœa, frequency of micturition, or dysuria. She was curetted one year ago. Did not alleviate the pain, nor did any pregnancy follow.

*Examination.*—*Heart and lungs.* Nil abnormal.

*Abdomen.*—Soft, definitely tender over MacBurney's point. No mass palpable.

*Vaginal examination.*—Cervix small. Pointing downwards and forwards. Uterus retroverted, normal in size. Right ovary palpable, slightly larger than normal. No tenderness or mass palpable in the right fornix. Left fornix—ovary palpable—larger than normal.

*Urine.*—Nil abnormal.

*Hb.* 65 per cent.

*B. P.* 125/80.

27th July, 1937. Under spinal anæsthesia laparotomy performed. Abdomen opened through mid-line sub-umbilical incision. Uterus found retroverted and both ovaries cystic. Tubes normal and patent. Appendix kinked and held down by adhesions about its centre. The tip bulbous—chronically inflamed. Appendicectomy and Gilliam's suspension performed. Abdomen closed in layers.

*Remarks.*—A case of sterility with retroverted uterus, cystic condition of ovaries, and chronic appendicitis.

Laparotomy was decided upon as she seemed to have definite signs of a chronic appendicitis. The uterus also was retroverted and rather fixed and as she was sterile and desired a child an anteverting operation was considered indicated. A definitely chronic inflamed appendix was removed and Gilliam's suspension done. The ovaries had small multiple unruptured follicular cysts on them. This was considered to be caused by the retroverted position of the uterus.

There was some difficulty post-operatively with getting her bowels open and starting normal micturition. Other than this she made an uninterrupted recovery.

*Case V.*—Age 27 years; race Hindu; married 12 years; number of children, nil; number of abortions, nil.

Admitted 31st January, 1938.

*Present history.*—Complains of sterility. Has no backache but has had dyspareunia since marriage. Has always had dysmenorrhœa which used to be at the beginning of the period only, but lately has continued throughout the period. No trouble with micturition. Not constipated.

*Periods.*—28/4-5 days. Painful throughout. Moderate loss. Last period seven days ago. She has had white discharge for the last twelve years.

*Examination.*—*Heart, lungs and abdomen.* Nil abnormal.

*Vaginal examination.*—Cervix pointing downwards and forwards. Os closed. Uterus retroverted, normal in size. Cannot be anteverted. Both ovaries palpable. Normal in size and prolapsed.

*Urine.*—No albumin. No sugar. 1020 acid.

*Hb.* 85 per cent. *R. B. C.* 3.9 million. *W. B. C.* 4400.

*B. P.* 120/80.

4th February, 1938. 9-30 a.m. Under spinal anæsthesia laparotomy performed. Abdomen opened through mid-line sub-umbilical incision. Uterus found retroverted, normal in size and appearance. Both ovaries had numerous small cysts over them. Both tubes tested and found patent. Uterus brought forward by Gilliam's technique. Abdomen closed. Dilatation and curettage performed.

18th February, 1938. Patient discharged after satisfactory progress.

*Remarks.*—This was a case of a woman married for twelve years with absolute sterility.

On account of this and the dyspareunia it was decided to antevert the uterus by operative means. This was carried out. What were taken to be unruptured follicles were found in both ovaries—due possibly

to the prolapsed state of these organs. Thus it was inferred that the sterility was due to the mal-position of the uterus and the effect of this on the ovaries. She made an uninterrupted recovery.

*Case VI.*—Age 37 years; race Hindu; married 30 years; number of children 3; number of abortions 1; last child 10 years ago.

Admitted 18th April, 1938.

*Present history.*—Complains of left-sided abdominal pain—10 months' duration. Pain is made worse by the periods, and lasts throughout the period. Pain has no relation to taking of food, but she often vomits food. No blood in the vomit. She is chronically constipated. No pain or blood on defecation.

*Periods.*—Last period 10 months ago. Periods before this were irregular, usually about every fifteen—twenty-five days. Each lasted about six days. Not profuse. She has left-sided pain during the period. Leucorrhœa—present. Has had this about five years, not offensive and has become more profuse lately. No pruritus.

She was in hospital last month, but left at her own request two days later, and has been having treatment for erosion in the out-patient department.

*Examination.*—Ill-nourished anæmic patient.

*Heart, lungs and abdomen.*—Nil abnormal.

*Vaginal examination.*—Cervix pointing downwards and forwards—erosion present—small. Uterus retroverted—larger than normal, fixed. Tender. Second degree tear of perineum.

There is some thickening felt in left fornix—tender.

*Urine.*—No sugar or albumin. No deposits or pus cells.

*Hb.* 60 per cent.

*B. P.* 115/85.

23rd April, 1938. Under spinal anæsthesia sub-umbilical mid-line incision made. Great omentum adherent by a long band to fundus of the bladder. This band was divided and removed. Uterus was retroverted, larger than normal and fixed by adhesions to the rectum and pouch of Douglas. Left ovary was non-existent except for a small cyst, the size of a hazel-nut. The distal half of the left tube was also non-existent. The proximal half seemed to be merged into the round ligament and the top of the broad ligament. The right tube and ovary were normal. Left ovarian cyst resected. The uterus was freed from its adhesions and Gilliam's method of suspension performed. The appendix was found tightly bound down by adhesions and kinked. Appendicectomy performed, abdomen closed in layers.

The perineal tear was repaired by a posterior colpo-perineorrhaphy.

7th May, 1938. Patient discharged fit. Temperature normal, wound healed.

*Remarks.*—This was a case of a woman with left-sided abdominal pain, irregular periods, and menorrhagia.

As her uterus was fixed and tender and there was diffuse thickening present in the left fornix, the symptoms were ascribed to a chronic inflammatory state of the pelvis causing adhesions.

A laparotomy was decided upon with a view to freeing the pelvic organs. The findings at operation were in agreement with the pre-operative diagnosis. She had all the late results of a healed general pelvic inflammation plus signs of old trouble in her appendix. The uterus was freed and anteverted by Gilliam's operation, the cystic left ovary removed and appendicectomy performed. She made an uninterrupted recovery.

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## THE RELATION OF LIVER TO OTHER DISEASES WITH SPECIAL REFERENCE TO GASTRO-INTESTINAL DISORDERS AND THEIR TREATMENT WITH INTRAVENOUS CALCIUM

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THERE is no other organ in the body which possesses so many functions as the liver. It is only recently we have begun to understand more about the functions of this important organ and even at the present stage of our knowledge we know very little. In the *Unani* and *Ayurvedic* systems of medicine the liver is believed to play a very important part in the aetiology of various diseases. It is not an uncommon experience to find the liver being blamed by physicians of indigenous systems for almost any ailment that a human being is liable to suffer from. The *Hakims* have believed for centuries that the liver plays an important rôle in the causation of gastro-intestinal disturbances, diabetes, anæmia, gout, asthma, hæmorrhagic diathesis, nephritis and œdema.

These conceptions of the functions of the liver have been based on the traditional belief and careful clinical observations of the old *Hakims*, although they possessed no diagnostic tests to help them. Recent advances in our knowledge of the physiology and pathology of the liver have made us respect these conceptions. It is beyond doubt that the liver plays an important rôle in gastro-intestinal disorders, pernicious anæmia and diabetes mellitus. Since the work of Heyd in 1924 on the relation of liver to kidney disease, a good deal of work has been done on the hepato-renal syndrome. Although the exact mechanism by which disorders of the liver cause kidney symptoms is not known, it is abundantly clear that some deaths from renal failure may actually be due to liver disease.

Girbal (1936) claims that in all asthmatic cases, if systematic search is made, signs of hepatic insufficiency can be found. He reports favourable results with liver extracts and

chologogues in such cases. Chrometzka (1936) has shown in animals that disturbance of purine metabolism can be produced by damaging the liver, with the result that the animal gradually loses the capacity to oxidize uric acid. He believes that similar mechanism may be responsible for gout in man, thus blaming the liver for another metabolic disorder the pathogenesis of which still remains a controversial point.

As the presence of bile in the intestines is necessary for the absorption of many fat-soluble vitamins as well as calcium, it is easy to understand the importance of liver disease in the causation of many functional and metabolic disorders due to avitaminosis and hypocalcæmia.

More recently it has been shown that liver disease causes a lowering of the prothrombin level of the blood and thus plays a very important rôle in the production of hæmorrhage. Hawkins and Brinkhons (1936), in studying the hæmorrhagic state induced by complete biliary fistula in dogs, have noted a deficiency of prothrombin and showed that it could be corrected by the administration of bile. It is likely that the hæmorrhagic state associated with liver disease is attributable to failure of absorption or utilization of some substance normally present in the diet which requires bile for its assimilation. This substance may be the hypothetical coagulation vitamin K, for Dam and his co-workers have shown that chicks fed on a diet deficient in this vitamin developed hæmorrhages in various parts of the body and this bleeding was associated with a decrease in the concentration of prothrombin of the blood. Clinical experiments with vitamin K, and bile salts by mouth in human subjects suffering from hæmorrhages seem to confirm the findings of Dam and his co-workers.

### *The rôle of the liver in gastro-intestinal disorders*

One of the oldest known functions of the liver is its rôle in digestion. The presence of bile in the intestines is necessary for the digestion and absorption of fats and fat-soluble substances. In obstructive jaundice the appearance of gastro-intestinal disturbances needs no explanation. But the symptoms of furred tongue, lack of appetite, gaseous distension of the stomach and intestines and irregularity of the bowels in cases of mild hepatitis without any apparent decrease in the production or flow of bile is difficult to explain. Whether these symptoms are due to insufficiency or poor quality of bile or to some other factor is not clear. The frequency of gastro-intestinal disturbances associated with minor disorders of the liver appears to be much more common than is realized. Careful observation of such cases has convinced the writer that these symptoms have little to do with cholecystitis with or without stones, for none of these cases has shown any definite symptoms of

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gall-bladder disease. Besides, the therapeutic measures which have proved successful in the majority of such cases have been directed mainly towards the improvement of liver function.

Furthermore the reasons for attributing these gastro-intestinal disorders to liver dysfunction are enlargement and tenderness of this organ and the disappearance of the gastro-intestinal symptoms as the liver recedes back to its normal size.

I have not been much impressed with the liver function tests which are often negative even when there is definite enlargement and tenderness of the liver. There is no reliable single test which can help in the diagnosis of minor grades of liver disorders. In fact animal experiments have shown that most of the commonly used tests remain negative even when more than 80 per cent of the liver is removed. Hurst (1937) believes that the *lævulose* test is perhaps the most valuable liver function test while in America the bromsulphthalein test is considered to be more reliable in the absence of jaundice. In my own limited experience the *lævulose* test has more often given me information about liver disease when all other tests such as bromsulphthalein test, Takata-Ara test, icterus index, van den Bergh reaction and urobilin in the urine have been negative.

As a matter of fact there is no point in performing elaborate liver function tests where the organ is enlarged and tender, for in all probability the liver is not normal in the majority of such cases. In those cases, however, where the liver is not enlarged or tender, liver function tests, if positive, are of great diagnostic value, but if negative they do not exclude the possibility of liver disease. Case 9 described later is of particular interest as the liver was neither enlarged nor tender but the *lævulose* test was positive when all the other tests were normal. As the case improved with calcium therapy the *lævulose* test also became normal.

The majority of such cases belonged to a better class or at least those who could afford to indulge in overeating, especially of meat and fatty and highly seasoned food. Alcohol did not play any significant rôle in the present series of cases, in fact most of these patients took no alcohol. Repeated pregnancies and prolonged lactation were additional factors in women, as they helped to drain the calcium of the body and also to the fact that some form of hepatic damage during pregnancy is not uncommon in this country.

The main symptoms complained of were lack of appetite, dyspepsia, wind in the stomach and intestines, constipation and sometimes diarrhoea, and general debility. Their history disclosed a varying period, from one to many years, of wandering from one consulting room to another but without much benefit. One case had been suffering for the last 7 years and had tried all kinds of treatment without any improvement.

Physical examination of these cases showed a pale complexion without jaundice or anæmia, furred tongue, and enlargement and tenderness of the liver. In the majority of the cases the liver was enlarged by one to two fingers but it was not rare to find a liver enlarged by 4 to 5 fingers. Some of the cases had low pyrexia especially when the liver was much enlarged. The most important physical sign was furred tongue. I have not come across a single case of hepatic indigestion with a clean tongue.

The hepatic syndrome has to be differentiated from other causes of liver enlargement, especially cardiac failure, amœbic and syphilitic hepatitis, gall bladder disease. The only condition which simulates this syndrome closely is active congestion of the liver of the tropics, but the absence of alcohol and long history are against such a diagnosis. When the liver is much enlarged in middle-aged or elderly patients the condition has been often diagnosed as cancer of the liver.

#### *Therapeutics of liver disorders*

The chief remedies prescribed in such cases are laxatives, bismuth, alkalis, carminatives, strychnine and other bitters, hydrochloric acid, taka-diastase, pepsin, kaolin, charcoal and very rarely bile salts. It is apparent therefore that the failure to get any substantial relief from such therapeutic agents is due to the fact that the primary cause does not lie in the stomach, intestines or gall bladder, for which the above drugs are prescribed.

The therapeutics of liver dysfunction and disease, when not due to any specific cause such as cardiac failure, syphilitic or amœbic infection, are not clear. Among the many drugs which have been advocated, and without much pharmacological basis, are calomel and other so-called cholagogues, ammonium chloride, salicylates, etc. Hexamine is used when there is co-existing cholecystitis, while bile salts, magnesium sulphate, olive oil and more recently nitrites are employed, when bile does not reach the intestines in sufficient quantities due either to insufficient production or as a result of stagnation in the biliary passages from spasm of the common bile duct.

The experiments of Mann, Bollmann and their co-workers have shown that the fatal toxæmia that follows the administration of hepatotoxic agents to dogs is greatly minimized by the prophylactic administration of diets containing large amounts of carbohydrates. Animals which were given high meat or high fat diet died very quickly. The experimental evidence is, therefore, greatly in favour of giving low fat and meat, and high carbohydrate diet to patients suffering from liver disease and in urgent cases large doses of glucose (200 gm.) have been given intravenously with considerable success.



In addition to the above drugs calcium has been recommended as a prophylactic against liver injury sometimes caused by carbon tetrachloride. In 1928 Lamson, Minot and Robbins discovered that calcium deficiency increased the liability to toxic degenerative changes in the liver by carbon tetrachloride. They found that dogs which were given high calcium diet succumbed less readily to the toxic action of carbon tetrachloride on the liver than the dogs on low calcium diet. It occurred to me that as calcium prevents the toxic action of carbon tetrachloride on the liver it might be useful in the treatment of other liver diseases. The results obtained have been most gratifying in the majority of cases while partial relief has been obtained in others. A recent personal communication with Drs. Bollmann and Snell of the Mayo Foundation, Rochester, U. S. A., shows that these workers have also used calcium gluconate in acute necrosis of the liver, but the results were not very promising. They, however, admit that they have not given calcium a fair trial and besides they were concerned mainly with experimental acute necrosis in animals.

The exact way in which calcium acts is not clear. Lamson, Minot and Robbins have put forward an hypothesis that the acute symptoms of calcium lack, such as characteristic tetany, tremors, convulsions and a great tendency towards hæmorrhage which follow carbon tetrachloride poisoning in dogs, are due to inactivation of the ionized calcium by its conversion into a complex un-ionized molecule with bilirubin, which circulates in large quantities after hepatic damage. While this hypothesis explains the symptoms of calcium lack it does not throw any light on the exact mechanism by which calcium prevents the toxic action of carbon tetrachloride on the liver.

In the present series calcium was given in the form of calcium gluconate, 10 per cent solution in doses of 10 c.cm. intravenously, every day for 5 to 15 days. If it did not cause any reduction in the size of the liver nor any amelioration in the symptoms within 10 days it was given up. No calcium preparation was given by mouth on account of its constipating effect and also because calcium absorption from the alimentary canal is very uncertain.

The diet was strictly restricted as regards meat and fats while carbohydrates and fruits were encouraged. This regime was not liked by most individuals and there was consequently some loss of weight in the beginning. Lately I have allowed these patients more liberal diet, especially skimmed milk, curd and about half to one ounce of butter per day for cooking purposes.

So far 25 cases have been treated on these lines with complete success in 17, partial in 6 and failure in 2. Both the cases which calcium failed to relieve as regards their main complaints it had a decided effect on the liver, which was reduced in size and tenderness by more than

fifty per cent. A record of 9 typical cases is given below :—

#### *Illustrative cases*

*Case 1.*—Mrs. C. D., aged 45, was referred to me in February 1938, suffering from anorexia, jaundice and fever with enlargement of liver of 2½ months' duration. She had been treated with purgatives, emetine injections, carbarsone and liver extract by mouth without any improvement and finally was diagnosed to be suffering from cancer of the liver. For the last fortnight her jaundice had become a little less and the pain in the right hypochondrium was also somewhat diminished. Physical examination showed her to be considerably emaciated, with moderate jaundice and œdema of the feet. Tongue was thickly furred and liver enlarged by three fingers and tender but soft and smooth on deep palpation. There was slight anæmia of a microcytic type. Examination of other systems did not reveal any abnormality. The stools and urine were normal except that the latter contained bile. Bile pigment was not absent from the stools. Temperature chart showed low grade fever ranging from 99.5° to 100°F., very rarely reaching 101°F. in the evening.

The fact that the jaundice was not progressive and that the dull and aching pain in the liver area had somewhat decreased lately made me rule out the possibility of malignant disease. With a history of sufficient anti-amoebic treatment proving ineffective a diagnosis of simple hepatitis was made and treatment commenced with parenteral calcium gluconate, large doses of glucose by mouth and meat- and fat-free diet. In the beginning ten units of insulin were given once daily for a week but later it was given up. She made slow but definite improvement, and after 20 injections of calcium gluconate given during five weeks her jaundice disappeared completely and the liver was only one finger enlarged. She was still suffering from some pyrexia, the maximum being 99.5°F., but another course of five injections of calcium gluconate brought her temperature down to normal. When seen six months later she had put on 21 pounds in weight, had a clean tongue and the liver was only just palpable on deep inspiration.

*Case 2.*—Mr. C., aged 82, was admitted into the Albert Victor Hospital, Lahore, in August 1938, with pain in the right hypochondrium, anorexia, fever of two months' duration and enlarged liver. He looked emaciated and the tongue was furred, the liver was enlarged by four fingers and tender but there was no jaundice. The temperature ranged from normal or 99°F. in the morning to 101–102°F. in the evening. Leucocytes 11,800. Differential count: polymorphonuclears 76 per cent, lymphocytes 20 per cent, large mononuclears 3 per cent and eosinophiles 1 per cent. Red corpuscles 3,500,000. Hæmoglobin 65 per cent. van den Bergh test negative. Stool free of helminthic ova and protozoal cysts. Urine contained traces of albumin but otherwise normal and did not contain any bile pigment. Other systems were normal. The general look of the patient, his age and marked enlargement of the liver suggested malignant disease, in fact he was sent to the hospital for this reason as all the usual forms of treatment had failed to improve him. In spite of this possibility calcium therapy was commenced. He was given 10 c.cm. of 10 per cent calcium gluconate intravenously daily. After two injections the tongue looked cleaner, the liver was definitely reduced by one finger and was not so tender and the temperature was also lower. On the 9th day the temperature remained normal throughout the day, the tongue was perfectly clean and the liver was only just palpable on deep inspiration. He was discharged on the 13th day. Enquiries made two months after his discharge showed that he was perfectly fit.

*Case 3.*—Mr. C. H. M., aged 40, was admitted into the Albert Victor Hospital, Lahore, in August 1938, with a history of ten days' fever. Physical examination showed no abnormality except a dirty tongue and two fingers' enlargement of the liver, which was also tender on



pressure. He looked pale but not jaundiced and the bowels were confined. Blood smears were negative for malarial parasites and the various laboratory tests for enteric group of fevers were also negative. Stools and urine were normal on microscopical as well as on cultural examination. He was given calomel and saline and diaphoretic mixture but without any improvement.

On the 4th day after admission calcium injections were commenced, with the usual dietary restrictions. The temperature became normal after the second injection, the tongue was less dirty and the liver was reduced by one finger. Three more injections of calcium gluconate brought the liver to its normal size and the patient regained his normal appetite whereas before he hated the sight of food. He was particularly pleased about his tongue which used to remain dirty ever since he came to India. When seen eight months later he was perfectly fit.

**Case 4.**—Mr. J. R., aged 35, was first seen by me in August 1938, for pain in the epigastrium, indigestion, loss of appetite and constipation of one year's duration. He looked a pale, thin and weak individual. The tongue was thickly coated and liver was tender and enlarged by three fingers. There was no jaundice and the stools and urine were normal. He had had mild pyrexia on and off for the last few months. Other systems were normal. He had been diagnosed and treated for abdominal tuberculosis but without any benefit.

He was put on meat-free, low fat and high carbohydrate diet and was given calcium gluconate in doses of 10 c.cm. of a 10 per cent solution daily. Improvement was prompt, the tongue cleared up within four days, the appetite returned, pain in the epigastrium disappeared and the liver became smaller. He was advised four more injections and was told to continue with his diet for another month. Seen four months later he looked very fit, was no longer pale and the liver was not palpable. He had gained nine pounds in weight.

**Case 5.**—Mr. S. R., aged 38, was treated by me in the Mayo Hospital for chronic amoebic dysentery with emetine bismuth iodide in July 1937. He had improved a good deal but came again in October 1937, with a relapse. His stools, however, were now negative for any *Entamoeba histolytica* cysts. He was given a course of carbarsone but without any improvement. Examination of his gastric contents after alcohol test meal showed hypochlorhydria and he was advised vitamin B<sub>1</sub> injections and hydrochloric acid by mouth. When seen again in October 1938, he was still complaining of indigestion and irregularity of the bowels. Examination of stools again did not show any *Entamoeba histolytica* cysts but now the stools contained *Giardia* cysts. He was given a course of atebirin 0.1 gm. b.d. for one week and further examination of the stools did not show any *Giardia* cysts but his symptoms remained the same. He was placed on calcium gluconate therapy as his liver was found to be tender and one finger enlarged and the tongue was coated. After five injections his liver was only just palpable and not tender but his tongue remained furred and the symptoms of indigestion and wind in the abdomen remained uninfluenced. He was given another course of five injections of calcium together with vitamin B<sub>1</sub> in 10 mgm. doses parenterally, and potassium bromide gr. 5 with luminal gr.  $\frac{1}{2}$  twice daily after meals but without any benefit. This case offered an unusually difficult problem for all treatments had failed to relieve him although calcium was effective in reducing the hepatic enlargement.

**Case 6.**—Mr. M. B., aged 40, consulted me in October 1938 for attacks of giddiness, sensation of heaviness in the frontal and malar regions, lack of appetite, distension of the abdomen after meals and constipation with alternating diarrhoea of four years' duration. He had consulted various physicians and *Hakims* and had swallowed many medicines and concoctions during the last four years. Examination showed a sallow-looking man of average build with a furred tongue and tender and enlarged liver (2½ fingers).

Other systems were normal and there was no pyrexia. He was placed on the usual high carbohydrate low protein and fat diet and was given calcium gluconate in 10 c.cm. doses daily. When seen five days later the liver was only one finger enlarged, the tongue was cleaner but the appetite had not improved much. He was advised another course of five calcium injections together with vitamin B<sub>1</sub> in 10 mgm. daily doses parenterally. When seen a week later he looked very cheerful, the tongue was clean and the liver was only just palpable on deep inspiration. He was particularly pleased with his appetite and began to enjoy his meal as he had not done for years. He, however, felt a little weak and was therefore allowed a little meat, and the fats were increased. When seen one month later he said he felt much better although 5 to 10 per cent of his trouble was still there. He was given another course of calcium and vitamin B<sub>1</sub> injections but without further improvement. When seen six months later he was still keeping fit and was not taking any medicine.

In this case vitamin B<sub>1</sub> must have been responsible for the increased appetite but it is likely that the reduction in the size of the liver was due more to calcium than vitamin B<sub>1</sub>. Failure to cure him completely was perhaps due to structural changes in his gastro-intestinal tract and some fibrotic change in the liver.

**Case 7.**—Mrs. K. K., aged 45, consulted me on 15th March, 1939, for low grade fever, anorexia and insomnia of one month's duration. Two years earlier she had bilateral pleurisy, ascites, oedema of the feet and high fever for which she was treated in hospital for nine months. She made a good recovery but after discharge from the hospital she continued to feel weak and had low fever for nearly three months. For the last year she was without fever and was feeling quite well until one month earlier when owing to domestic worries she lost her appetite and developed fever again.

She was a thin and pale-looking woman with a worried look. The tongue was furred and the liver enlarged by two fingers and tender on pressure. Spleen was also enlarged by one finger and hard, suggesting a chronic enlargement. Examination of other systems including stools and urine did not reveal any abnormality, except that the blood pressure was of low tension (110-80). Given calcium gluconate intravenously and after the second injection the liver was much less tender and only one finger enlarged. The tongue was still furred and the bowels which were regular became constipated. The fever was less and the pulse was better. She also slept well for the last two nights. After the 4th injection she developed high fever and felt drowsy all that afternoon and night. The temperature came down next day and she felt much better, the appetite was greatly improved, the tongue was cleaner, the liver was one finger enlarged and was only slightly tender on deep pressure. Two more injections of calcium gluconate further reduced her liver but the second injection gave her high fever again. Next day she contracted bacillary dysentery and the treatment was stopped. After ten days' absence she turned up again and was given a course of five more injections of calcium gluconate. This improved her greatly. When examined on 25th April, 1939, the tongue was clean, liver just palpable on deep inspiration and not at all tender, the appetite was normal, sleep good. She was no longer pale and had no fever since she stopped calcium injections. She was given more liberal diet and when seen three weeks later was quite well and free from all symptoms.

**Case 8.**—Mrs. M. D., aged 44, was referred to me in October 1938, for attacks of pain in the right hypochondrium radiating to the back, dyspepsia, eructations, excessive salivation and anorexia of seven years' duration. For the last year the symptoms had become worse and in spite of various forms of treatment she was no better. Examination showed pale complexion without jaundice, furred tongue with tender and enlarged liver (two fingers). The liver was more tender near the gall bladder region. She was given large

doses of hexamine and alkalis with tincture belladonna but it did not give her more than 20 per cent relief. She took these medicines for six weeks without further improvement. She was then given 5 per cent of calcium chloride in 20 c.cm. doses intravenously for four days but without much benefit although examination of the liver showed definite reduction in size (one finger) and tenderness on deep pressure. The last injection gave her considerable pain in the arm and she discontinued the treatment for about four months. She came again in March 1919, and was given intravenously 50 per cent glucose in 50 c.cm. doses daily instead of calcium. After five injections she felt considerable relief and the attacks of pain became less severe. She was given five more injections of glucose during the next ten days. After this the tongue became clean, the liver was no longer tender nor enlarged, complexion became normal and she felt very cheerful. The attacks of pain in the hypochondrium and the back were much less frequent and severe. She was advised to take one tablet of nitroglycerine, gr. 1/100 to be sucked when the attack came. After two months she was still feeling very well and did not complain of any trouble. Seen on 4th January, 1940, she was still keeping fit without any medicine.

This case probably had cholecystitis in addition to hepatitis. It is difficult to say whether more injections of calcium would have improved her as much as glucose.

Case 9.—Mr. M. A., aged 29, a medical man, consulted me on 8th May, 1939, for general weakness, loss of weight and anorexia since January 1939, when he developed an attack of catarrhal jaundice. The jaundice which was unaccompanied by fever or enlargement of liver persisted for two months despite all treatment and then gradually diminished and disappeared completely by the beginning of April 1939. Previous to this he had suffered in 1927 from enlarged liver (one finger), irregular rise of temperature and loss of weight. The diagnosis was hepatitis and the treatment consisted of the use of mild purgatives such as sodium phosphate and small doses of magnesium sulphate, podophyllin and euonymin and restricted diet. The disease lasted for six months but the patient continued to take these medicines for several years, as whenever he gave them up he lost his appetite and weight.

Physical examination showed no abnormality except a pale and lean individual with furred tongue. The liver was not palpable and there was no jaundice. In view of the history of hepatitis and a recent attack of jaundice it was decided to perform the liver function tests, especially as the liver was neither enlarged nor tender on deep pressure.

Bromsulphthalein test—Negative.

Icteric index—9.

van den Bergh test—Negative.

Urobilin test—Negative.

#### LÆVULOSE TEST

Time in hours	Blood sugar mg., per cent	Urine sugar
0	96	Nil.
1	126	Nil.
2	100	Nil.
3	86	Nil.

In view of the positive lævulose test it was decided to give him a course of calcium injections. He took ten injections of 10 c.cm. calcium gluconate (10 per cent) for ten days and afterwards took 30 grains of calcium gluconate twice daily by mouth for 20 days. During injection therapy he felt well and did not feel tired. The tongue became less coated and the appetite was definitely improved. The stools which were somewhat loose became regular and well formed. The weight, however, remained stationary (110 pounds).

After one month's treatment the lævulose test gave the following figures:—

Time in hours	Blood sugar mg., per cent	Urine sugar
0	105	Nil.
1	125	Nil.
2	110	Nil.
3	95	Nil.

The above case is interesting in that the lævulose test showed liver insufficiency when there was no enlargement nor tenderness of the liver and also that calcium therapy improved the liver function as shown by the second lævulose test.

#### Discussion

The importance of liver disorders as the cause of metabolic and gastro-intestinal disorders is becoming more evident. A large number of cases of indigestion, lack of appetite and irregular action of the bowels are due to deranged liver function. Some of these cases suffer from low grade pyrexia which may persist for many years, and offer considerable difficulty in diagnosis. If the liver is kept in mind it is easy to diagnose these cases, the criteria being enlargement and tenderness of the liver, when the ordinary causes of enlargement of this organ are excluded. There are probably other cases with similar symptoms but without an enlarged or tender liver such as case 9, but their diagnosis at present is difficult because, with the doubtful exception of the lævulose test, the liver function tests are not delicate enough to detect minor grades of liver disorders.

The treatment of gastro-intestinal disorders secondary to hepatic disease has been far from satisfactory in the past. This is partly due to lack of appreciation of minor grades of liver dysfunction as the cause of such disorders and partly because the average physician does not seem to be fully acquainted with the pharmacology of the liver.

Although the present series of cases are too few to form a definite conclusion about the efficacy of calcium in liver disorders, by the encouraging results reported in this paper it is hoped to stimulate further work in this direction.

My thanks are due to Mr. B. D. Kochhar, M.Sc., and Dr. Abdul Qayyum Malik for the help they rendered me in carrying out this work and Dr. K. A. Hameed of the 'Cipla' Ltd. for supplying me with liberal samples of his 'Calcima' brand of calcium gluconate.

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PROPHYLACTIC ANTI-RABIC VACCINE  
FOR ANIMALSBy W. J. WEBSTER, M.C., M.D., D.P.H., D.T.M. & H.  
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SMITH *et al.* (1938) reported an experiment which suggested that a popular proprietary anti-rabic vaccine for animals given by the 'one-shot' method affords less protection to street virus infection than does the Kasauli vaccine given by the seven-dose method recommended. As the numbers of animals used in this experiment were rather small it was proposed to repeat the comparison on a much larger scale using both dogs and monkeys. The matter is one of some practical interest.

Anti-rabic vaccine experiments with dogs have been notoriously unsatisfactory in the past and this attempt was no exception. In fact the experiment had to be abandoned because out of 120 dogs originally employed all except 42 died of 'other causes', mainly distemper.

Brown monkeys, *Silenus (Macacus) rhesus*, weighing about 20 lbs., were divided into three groups of 23 animals each. The monkeys of the first group were given the Kasauli 6 per cent sheep's brain carbolized vaccine in seven daily subcutaneous doses of 5 c.cm. each. On the seventh day the monkeys of the second group were given one dose of the proprietary vaccine. The third group of monkeys received no treatment. One hundred days after completion of this treatment all the 69 monkeys had injected into the deep muscles of the neck 2 c.cm. of a 2 per cent emulsion of the brain of a rabbit which was completely paralysed 15 days after intracerebral infection with the brain substance of a dog which had died of naturally acquired

rabies. Negri bodies were present in the brains of both dog and rabbit. The results of this experiment are shown in the table, the monkeys having been observed for a period of 98 days after the test dose of street virus was administered. In all cases of death from rabies the diagnosis was confirmed histologically.

TABLE

Prophylactic treatment employed	Number of monkeys tested	DIED	
		'Other causes'	Rabies
Kasauli vaccine ..	23	Nil	1
Proprietary vaccine ..	23	Nil	15
No treatment (controls)	23	1	13

It appears reasonable to conclude that the course of Kasauli animal vaccine affords better protection against street virus infection than the proprietary vaccine given by the 'one-shot' method. Repeated doses of the latter might give better results but the 'one-shot' method is popular in India and it appears desirable to report that this may not be adequate. No attempt is made to compare the two vaccines in terms of equal dosage of brain substance nor to assess the value of vaccine treatment after exposure to infection has occurred. This note merely contrasts the possible protective value, before infection, of two methods of prophylactic treatment which are in general use in India. The experimental results should be of interest to dog owners and to persons responsible for planning anti-rabic vaccine campaigns among dogs.

For several years an attempt has been made to collect figures regarding the anti-rabic treatment of dogs with Kasauli vaccine. Reports have, however, been received in respect of less than 60 per cent of the dogs inoculated. The consolidated figures for the three years 1936 to 1938 are as follows :—

Reports received in response to enquiries made  
six months after completion of inoculation

Total inoculated	DOGS INOCULATED AFTER EXPOSURE TO INFECTION		DOGS INOCULATED PROPHYLACTICALLY	
	Number	Deaths believed to be due to rabies	Number	Deaths believed to be due to rabies
4,349	767	18	1,838	1

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## WHEREIN LIES THE ACTIVITY OF SULPHANILAMIDE ?

By U. P. BASU, D.Sc., P.R.S.

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SINCE the development of modern 'Chemotherapy' by Paul Ehrlich, various synthetic compounds have been offered to clinicians for treatment of disease. Amongst these the compound—hydrochloride of 4'-sulphonamido-2,4-diaminoazobenzene—with which Domagk (1935) experimented was a remarkable advance because it extended Ehrlich's chemotherapy to the treatment of infections as yet not influenced by any chemical. Subsequent researches in this direction further show that, for the major portion of the bactericidal effect of the azo dye, the sulphanilamide grouping present is mainly responsible. Of course, there is now considerable difference of opinion as to whether sulphanilamide itself is or is not the sole active agent in this new therapy. Still, in view of the great therapeutic significance of sulphanilamide, extensive investigations have been carried out to discover its mode of action on the one hand, and to obtain a more effective but less toxic substitute on the other.

At the outset, it may be pointed out that the active radical common to all the drugs now in

use is  $N \text{—} \text{—} \text{—} S$ . But this does not mean

that the presence of nitrogen or sulphur is absolutely essential for the development of the chemotherapeutic activity, as Levaditi, Girard and Vaisman (1938) noticed an activity in dihydroxy diphenyl sulphone,— $(HO.C_6H_4)_2SO_2$ —, and Mayer and Oechslein (1939) in p-nitrobenzoic acid,  $p\text{-NO}_2.C_6H_4.COOH$ . The replacement of the amino group from the para to the other positions, or, the addition of amino or sulphonamido group in p-amino benzene sulphonamide molecule, however, lowers the efficacy of the drug. The substitution of the amino hydrogen of the p-amino group in sulphanilamide might either increase the solubility, lessen the toxicity, or both, but would not have any influence on the efficacy or the range of activity of the drug. The replacement of the amide hydrogen of the sulphonamido group by other radical or nucleus has again afforded a number of products that are equally, if not more, effective against infections affected by sulphanilamide itself, and in addition possess certain advantages over them in gonococcal and pneumococcal infections. The recent observations of Climenko, Crossley and Northey (1939) on the efficacy of the sodium salt of disulphanilamide in mice infected with a strain of human influenza virus, is of more than theoretical interest as it raises the possibility of influencing virus diseases with this group of drugs.

The question how and in which way the sulphanilamide or any of its derivatives produces

the therapeutic effect in bacterial infections, still remains unsolved. From general considerations the compound may exert its characteristic effect by being a simple disinfectant, by stimulating the natural defences of the body or by acting by a combination of these two factors. But unlike the well-known germicides such as acriflavine, brilliant green and others, sulphanilamide is neither instantly bactericidal nor even instantly bacteriostatic. The effect of sulphanilamide on the growth of micro-organisms is more pronounced in ordinary infusion broth in comparison with that in rabbit serum (Gay *et al.*, 1939). A review of the whole literature shows that the drug is bactericidal by some adjuvant factors [Nitti, Bovet and Depierre (1937), Finklestone-Sayliss, Paine and Patrick (1937), Lockwood (1938) and others]. The bacteriostatic as well as the bactericidal activity varies, not only with the type of culture, but also with the nature of the substrate. Sulphanilamide is active against streptococci *in vivo* but ineffective in peptone-containing broth at ordinary temperature. The activity in the latter medium may be restored by raising the temperature to 39 to 40°C. [White and Parker (1938), Weld and Mitchell (1939)]. The observation of Britton (1938), that it is active against pneumococcus type I in peptone-containing broth but practically inactive *in vivo*, makes the problem more complex.

One of the necessary conditions for its therapeutic action is that the organism and the drug should actually meet in the body of the host (Browning, 1939), as it does not set up any permanent anti-bacterial condition within the body. It may be mentioned that antiseptics like acriflavine are fixed by streptococci whereas the drugs of this group are neither changed nor fixed by contact *in vitro* with large masses of the bacteria. Still there exists a quantitative relationship between the concentration of the drug and the number of bacteria (McIntosh and Whitby, 1939). A higher concentration of the drug is effective against a greater number of organisms and a lower one against the smaller number. In all cases, however, a definite bacterial multiplication takes place at least for the first few hours. This feature—a 'lag' phenomenon—is invariably noticed in experiments whether carried out *in vitro* or *in vivo*. What is the cause of this delayed action? Is it due to the time required for a chemical transformation of the drug in the body or is the drug gradually entering into some chemical combination with the bacterial protein? That the drug does not act directly upon the micro-organisms is also evident from the observation of Levaditi and Vaisman (1938) that sulphanilamide is more potent when absorbed *via* the gastro-intestinal tract than when locally applied, or, when injected directly into the peritoneum for immediate contact with the infectious agent. Levaditi and Vaisman (1938a), from their study on the effect of the drug on bacterial endotoxins, have also suggested that the drug has to undergo a change

*in vivo* in order to exert its neutralizing action on the endotoxin. This is very difficult to reconcile with the conception advanced by Barron and Jacobs (1937) as well as by Chu and Hastings (1938) that the drug behaves in such a way that the organisms are unable to utilize the nutriment from the body of the host. Evidence is also lacking to show that the production of toxin by the bacteria is inhibited, or, if formed, then it is inactivated by the drug [Osgood and Powell (1938), Gross *et al.* (1938), Gay *et al.* (1939)]. Even the virulence of the micro-organism is in no way impaired by contact with the drug in a concentration as high as 1 in 2,000 (Browning, 1939).

The other point that may be considered is whether the drug has any stimulating action on the natural defences of the body. In clinical study, leucocyte counts do not show any variation other than the usual daily fluctuation, and consequently the drug does not stimulate leucocytosis [Gay and Clark (1937), Mellon *et al.* (1937)]. Osgood and Powell (1938) and Gay *et al.* (1939) have again observed no evidence of any marked opsonic action of the drug. The general belief now is that the production of antibodies is not stimulated and there is no direct action upon the phagocytic mechanism in the body of the host [Reid (1939), Traut and Logan (1939), McIntosh and Whitby (1939)]. It seems therefore that the drug, by one or other change, inhibits the growth of bacteria, and this necessarily causes a suppression of their aggressive character. Under such circumstances, the natural body defences may easily play their part and ultimately help in the immunity mechanism.

What, then, is the factor that contributes to the remarkable chemotherapeutic action of a group of drugs otherwise possessing a weak antibacterial property *in vitro*? It was Mayer (1937) who first suggested that the antistreptococcal effect of sulphanilamide might be due to some other substance produced from the drug *in vivo*, and considering the first product of oxidation of an aromatic amine to be the hydroxylamine, he pointed out that p-hydroxylaminobenzene sulphonamide is the active substance in this therapy. A rider to this hypothesis was further added by Locke, Main and Mellon (1938) from their belief that such an oxidation would enhance the anticatalase activity which sulphanilamide and several allied compounds were found to possess (Main *et al.*, 1938, Shinn *et al.*, 1938). Whether the hydroxylamino derivative is sufficiently stable or not in the system, its presence, though in very low concentration, is indicated from the recent experiments of Rosenthal and Bauer (1939) with urine of patients. But the anticatalase activity alone cannot truly explain the mode of action of this group of compounds (Long and Bliss, 1939). Harris and Michel (1939), from their clinical observations, have deduced that sulphanilamide is partially converted by the body into some

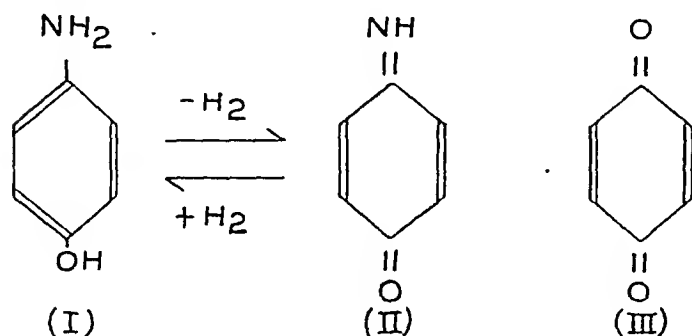
active agent which, functioning as an oxidant, is supposed to be responsible for the occurrence of methæmoglobinæmia in patients receiving therapeutic doses of the drug. As this formation of methæmoglobin is frequent both in adults and children, irrespective of the sex, it would not be unnatural to postulate that in its formation lies the factor on which the activity of the drug depends. In other words, is this oxidizing agent then simultaneously accounting for the toxic symptoms as well as for the therapeutic effectiveness of the drug? (Shaffer, 1939).

The most common toxic effects that have been reported following the use of this group of drugs have been nausea, vomiting, depression, dizziness, fever, headache, acidosis, cyanosis, decrease in hæmoglobin and red blood corpuscles. But the majority of these are not of such a nature as to contra-indicate the use of the drug. The most serious types of toxic manifestation are acute hæmolytic anæmia and agranulocytosis; but these rarely occur. Sulphanilamide causes an acidosis due to alkali deficit occurring from the loss of excess of sodium and potassium in the urine. It produces a decrease in pH of the blood and increase in the pH of urine (Long and Bliss, 1937 and 1937a). The administration of sodium bicarbonate prevents the occurrence of any clinical acidosis. But the most common symptom in patients receiving therapeutic amounts of sulphanilamide or, retaining 4 mgm. of sulphanilamide per 100 c.cm. of their blood, is the development of cyanosis, or, blueness of the skin (Wendel, 1938, Bensley and Wilen, 1939). It is invariably associated with the formation of methæmoglobin [Hartmann, Perley and Barnett (1938), Evelyn and Malloy (1938), Wendel (1938)] and occasionally with that of sulphæmoglobin (Colebrook and Purdie, 1937). Marshall and Walzal (1937), however, suggest that the cyanosis may not be due to any change in the condition of the blood pigment but may be due to the formation of an oxidation product of sulphanilamide (Ottenberg and Fox, 1938). The observations of Harris and Michel (1939) that the intensity of methæmoglobinæmia is proportional to the concentration of the drug, tends to show that the methæmoglobin formation during treatment is a definite action of the drug. Sulphanilamide itself cannot oxidize hæmoglobin *in vitro*, whereas in contact with body tissues it undergoes a change that is responsible for the production of methæmoglobin (Harris, 1939). Very recently Wendel, Wendel and Cox (1939), from their spectrophotometric and simultaneous gasometric analyses of fully oxygenated blood from cyanotic patients, have expressed the opinion that the pigmentation during sulphanilamide therapy is for the most part due to the formation of methæmoglobin.

Such a phenomenon is not a new one as various substances, *e.g.*, aniline, acetanilide, nitrobenzene, etc., have been found to cause cyanosis and methæmoglobinæmia *in vivo*, though they have no action on hæmoglobin



*in vitro* (McElroy, 1919, Scott and Hanzlik, 1920). Considerable differences of opinion exist regarding its mechanism, but the general belief now is that p-amino phenol formed in the system from the above aniline bodies is mainly responsible for this cyanosis [Heuhner and Schwedtke (1936), Schwedtke (1938), Michel *et al.* (1937), Harrop and Waterfield (1930)]. The p-amino-phenol (I) is readily oxidizable to p-iminoquinone (II) and this transformation being reversible, a small amount of either agent would produce many molecules of methæmoglobin.



In *in vitro* experiments sulphanilamide can be oxidized to quinone (III), when it would not be unreasonable to expect that an oxidation in *in vivo* may lead at least to the formation of p-iminoquinone (II). If this latter product be once formed in the body, it would establish an oxidation-reduction equilibrium with p-amino-phenol (I) and, as such, may be the cause of the oxidation of hæmoglobin to methæmoglobin (Rimington, 1939). On this basis, the formation of methæmoglobin would first depend on the ease of oxidation of sulphanilamide drugs to p-iminoquinone. In clinical practice, too, the rate of formation of methæmoglobin is found to be much lower in 2-(p-aminobenzene sulphonamido)-pyridine (IV) and p-benzylamino benzene sulphonamide (V), two products less susceptible to decomposition from chemical consideration [Harris and Michel (1939), Finland (1939)]. Acidosis, by interfering with absorption of alkalis in renal tubes, and an increase in the urinary excretion of porphyrin, are two other common physiological disorders during this chemotherapeutic treatment (Rimington and Hemmings, 1938). The two effects are again minimum in the case of compounds (IV) and (V), indicating thereby that the various toxic manifestations depend on one and the same factor. The injection of methylene blue (0.1 to 0.2 c.cm. per kilogramme of body-weight of a one per cent aqueous solution) removes the methæmoglobin from the circulating erythrocytes without any injurious effect on the host, and thereby restores the oxygen-carrying capacity of the blood (Wendel, 1939). This seems to be logical as this readily reducible dye, by disturbing the reversible reduction-oxidation equilibrium between the above two agents, would then inhibit the formation of any further quantity of methæmoglobin. Any conjugation of sulphanilamide would make it more resistant to

oxidation and this would in turn lessen the probability of any change in the hæmoglobin molecule. Such a conjugation has been actually found by Bensley (1940) to reduce the formation of methæmoglobin. All these then point to an alteration in the composition of sulphanilamide in the body. Further, the fact that the concentration of both free and acetylated sulphanilamide is invariably higher in the corpuscles than in the plasma, again indicates an existence of a close relationship between blood corpuscle and sulphanilamide (Hansen, 1939). It really suggests a sort of combination between something within, or on the surface of the corpuscle and the drug. As the method of estimation of distribution of the drug has been traced by means of diazo (colour) reaction with the p-amino grouping of the drug and no consideration is being made for the sulphonamido—SO<sub>2</sub>NH<sub>2</sub>—grouping, so the question remains unsolved whether the product that tends to be associated with the red blood corpuscles is the sulphanilamide molecule itself, or some product at least in part derived from it. The problem now is whether in such transformation lies the anti-bacterial activity of the drug in question. P-iminoquinone (quinoneimine) has been recently found by Bernheim *et al.* (1938) to inhibit the oxygen uptake of body tissues and the xanthine oxidase of liver. The action is dependent on the formation of a quinoneimine-enzyme complex. Does this also inactivate the bacterial enzymes (McIntosh and Whitby, 1939)? The mode of action of this group of drugs should then depend on the formation of p-iminoquinone and its subsequent conversion in such a way as to inactivate the invasive character of the micro-organisms. But the presence of such p-iminoquinone in the system will have to be demonstrated. The idea would not, however, preclude any sulphanilamide drug exerting its own characteristic pharmacological effects—whether therapeutic or toxic—depending on its ability to penetrate through the cell membrane and subsequent ease of oxidation to p-iminoquinone inside the cell.

It would be of much interest to study the exact chemical nature of the drug that is being daily excreted in the urine, circulated in the blood and more particularly remaining associated with the red blood corpuscles. The next point of importance seems to be a study on the effect of the drug on endotoxin *in vitro* in the presence of several body tissues under various conditions, and then to note the effect of such a mixture on treated and untreated animals. An investigation on the change, if any, in the constitution of the drug seems also to be essential. All these might bring forth a clue to the mechanism by which this group of drugs exert their characteristic pharmacological action, or, at least might throw light on the problem whether the oxidant that is invariably formed, exerts any influence on the anti-bacterial action of the drug. For such a study team work from



chemists, bacteriologists, biologists and clinicians is essential.

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## A Mirror of Hospital Practice

### A CASE OF CEREBRO-SPINAL FEVER CURED BY SULPHANILAMIDE\*

By BABU RAM GARG

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A boy aged 14 had an attack of 'fever' and headache on 16th March accompanied by frequent liquid stools. The temperature increased but was not recorded as a thermometer was not available.

I first saw him the following morning and found his axillary temperature 103.5°F., pulse 120 and respiration 20 per minute, sighing in character.

The patient was deeply unconscious—pupils fully dilated, equal and did not react to light, and reflexes were absent. There was no stiffness of the neck nor head retraction but pressure over the spine caused twitching of the face muscles indicating that it was painful.

Diagnosis was doubtful as at the time I had no needle to do a lumbar puncture and there were no similar cases in the village.

The boy could swallow liquids so he was given six doses of a hexamine mixture and six powders (half gramme each) of Septalium, Glaxo (a sulphanilamide product).

On 18th March, the condition was unchanged except that one pupil was now smaller than the other. The parents refused permission to do a lumbar puncture.

\* Rearranged by Editor.

The same treatment as on the previous day was continued with the addition of an intravenous injection of 5 c.cm. of 'Aktisol', a sulphanilamide drug.

On 19th March the boy was brought to my dispensary and on lumbar puncture 23 c.cm. of opalescent fluid under pressure was allowed to escape. Microscopically it contained large numbers of intracellular diplococci. The left pupil was more nearly normal and reacted slightly to light.

He was distinctly better on the 20th, consciousness was returning and the pupils were normal in size and reaction.

On the 21st, the boy was fully conscious. Lumbar puncture was again performed and 50 c.cm. of clear fluid evacuated under slight pressure. Diplococci in smaller numbers could still be seen. Reflexes were now obtainable.

The treatment was continued and there was steady improvement. On 23rd March 15 c.cm. of cerebro-spinal fluid was withdrawn and only very scanty diplococci could be seen. Progress was maintained and on 27th March 35 c.cm. of fluid was withdrawn; and no micro-organism could be found in it. The temperature was normal. Intravenous medication was stopped but Septalinum by mouth was continued. All treatment was stopped on 30th March and the boy was discharged as cured.

**Conclusion.**—An obviously severe case of cerebro-spinal meningitis was cured by means of sulphanilamide drugs.

## A METHOD OF REMOVING A TIGHT RING FROM A FINGER

By Y. M. BHAVE, M.B., B.S.

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It is not infrequently that the general practitioner comes across a patient with a ring impacted on one of the fingers. The following is a useful method of removing such a ring with the least amount of trauma to the tissues involved.

**Anæsthesia.**—It is better to block the digital nerves with 2 per cent novocaine or in the case of children just to give a little general anæsthetic, to keep them quiet. As a general rule very

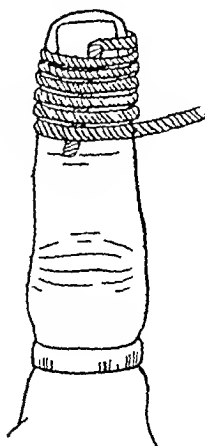


Fig. 1.

little pain is felt during the manipulations. The adrenalin content of the local anæsthetic reduces the congestion and makes the proceedings easier.

**Technique.**—First clean the part with rectified spirit. Starting at the tip of the finger (figure 1) a strong thread (twine would suffice) is

wound round the fingers, the strands touching each other without overlapping, till the strands reach in the vicinity of the ring. The free end of the thread is now manipulated under or preferably threaded through the ring with a vaselined aneurism needle, so as to come out at the proximal edge of the ring (figure 2). Any space,

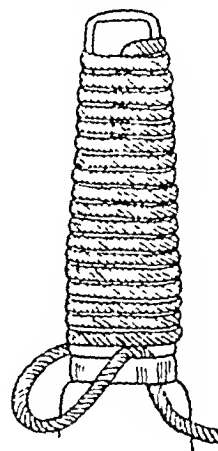


Fig. 2.

between the most proximal strand of the thread and ring, left uncovered is covered by continuing the winding, the loose proximal end of the thread being pulled so as to leave no loop between the ring and the fingers. Sterile vaseline is now applied to the ring and all the strands of the thread. The thread is now unwound, from the proximal end, a little force being usually necessary to do this (figure 3).

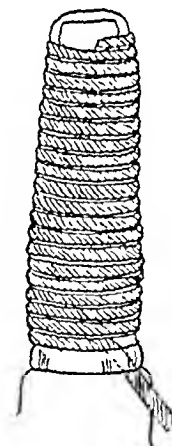


Fig. 3.

The ring will be found to move very slowly forward till it slips off the finger, when the whole thread is unwound. Thick cat-gut can be used but only if a sufficiently long strand is available, to enable the proceedings to be finished with only one winding and unwinding.

**Mechanism.**—This method works both by relief of congestion brought about by direct pressure of the thread, and by the screw-like action when the thread is unwound.

### ERRATUM

Our attention has been drawn to an error on p. 179 of the March number.

From 'Calcium diuretin' to 'Citobaryum' the names should be lowered one line to correspond with the correct particulars in columns two and three of the table.

# A Tonic and Reconstructive of Exceptional Efficiency

**Fresh Liver  
& Spleen**  
for bloodbuilding

**Cod Liver Oil**  
for its food value

**Malt Extract**  
for its nutritive influence

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for remineralization

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A bottle of each form is at your service.  
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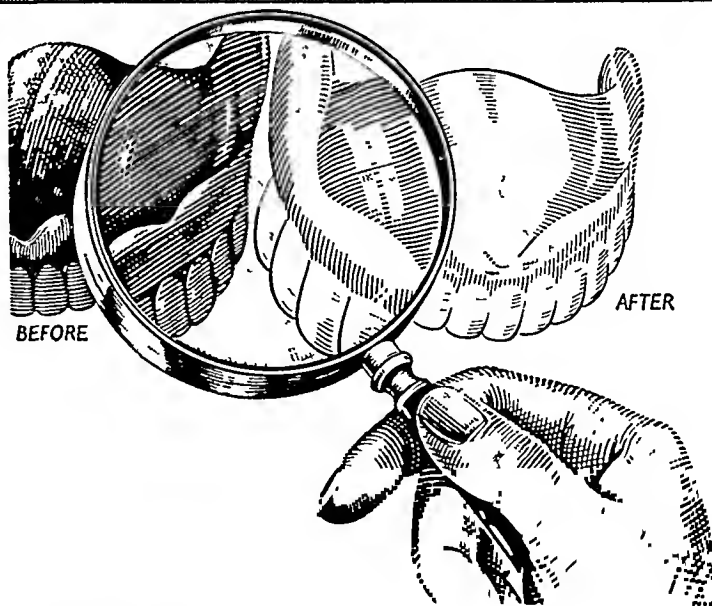
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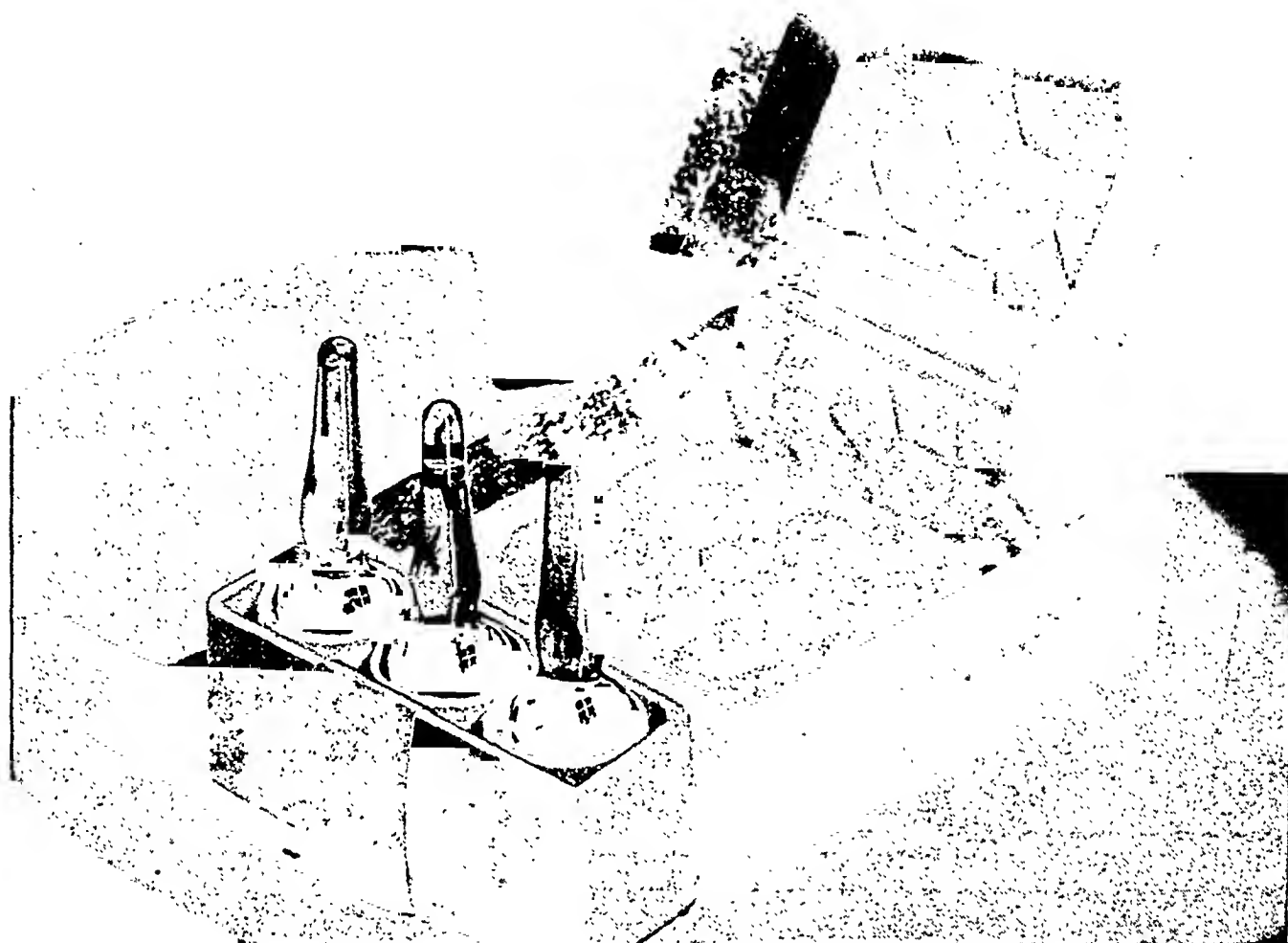
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# Steradent

REGD. TRADE MARK

**CLEANS & STERILISES FALSE TEETH**



# ANAHÆMIN B.D.H.

## In Nutritional Macrocytic Anæmias

Nutritional macrocytic anæmias are stated to be due primarily to a deficiency of Castle's extrinsic factor. It is logical, therefore, to assume that they will respond to the exhibition of Anahæmin—the product of interaction of intrinsic and extrinsic factors.

Convincing evidence of the value of Anahæmin in nutritional anæmias is provided in a report (Response of Nutritional Macrocytic Anæmia to Anahæmin, *Lancet*, August 12th, 1939, p. 360), in which it is shown that Anahæmin is at least as active in its curative effect as less highly-purified preparations of liver.

In other words, Anahæmin is of high and unvarying activity, not only in pernicious anæmia which is due to lack of intrinsic factor, but to nutritional anæmias which are due to lack of extrinsic factor. This latter fact accounts for the restorative effect produced upon patients after operation or who for one reason or another are maintained on a restricted dietary.

*Stocks of Anahæmin B.D.H. are held by leading chemists, and full particulars are obtainable from :*

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## Indian Medical Gazette

JUNE

### THE PROBLEM OF DRUG ADDICTION

Drugs of addiction are those which are liable, in the course of time, to take control of the individual who has become habituated to their use inasmuch as all his social and business obligations become subservient to obtaining a regular supply of his pet narcotic, and their continued use, generally in increasing quantities, to obtain the desired effect eventually leads to complete moral and physical degeneration and even death. This practice of taking drugs, not for the cure of disease but for their euphoric and stimulating effects, is one of importance as well as of considerable interest on account of the numerous problems involved.

The habit is so ancient and so widespread throughout the human race that it almost seems that man has an innate need for stimulo-sedatives of some kind. This is suggested by the fact that when European explorers first made contact with races who had been, as far as we know, completely out of touch with other races for immeasurably long periods of time, most of them were found to be using regularly some form of narcotic or stimulant drug. For example the natives of the South American jungles were accustomed to use cocaine in a crude form, and even in remote Australia the primitive and widely scattered nomads inhabiting this country had a plant of similar nature, which although very mild in its action was greatly prized and was of high trade value between parts of the country where it grew and those places where it was not found, so that it was passed from tribe to tribe over many hundreds of miles of sparsely populated country. In large parts of Asia and Africa Indian hemp has been used from as far back as records go, and it is probable that the practice began in the earliest stages of man's social development in these countries. Elsewhere in this issue there is a full summary of the subject of hemp drug addiction in this country, which embraces the earliest historical records of its use and traces it right up to the present day. This report is only an account of part of the general study of the use and abuse of drugs of addiction in India, which has been carried out by Colonel Chopra and his collaborators over many years, under a grant from the Indian Research Fund Association.

World communications have improved so much and trade ramifications have spread so widely that, now in times of peace, every country or state trades with every other one in the world, and all world products are obtainable almost

everywhere. This applies to narcotic drugs as well as to other commodities and manufactured articles, and those which were originally used almost exclusively in one country or area are now obtainable anywhere. The prevention of the traffic in narcotics is a large and important problem in most countries and one on which governments are compelled to spend vast sums of money. One of the most important countries in this respect is Egypt, which on account of its geographical situation, is a suitable clearing-house for drugs between Europe and Asia, quite apart from having a serious local problem of drug addiction of its own. As is always the case the demand has created the supply and one of the most active narcotic preventive services in the world exists in Egypt, and the work of this bureau is of great value outside its own borders because it has been able to indicate the source of origin of much of the drugs seized in that country. The world effort to limit the international traffic in dangerous drugs is greatly assisted by the League of Nations whose organization is well fitted for operations of this nature.

Before the days of rapid and frequent inter-communication throughout the world, in which every country now participates, different countries were prone to use one type of stimulo-sedative to the almost total exclusion of others. For instance, speaking in the broadest sense, Europe used alcohol, Asia used Indian hemp and later opium, North America used tobacco, South America used cocaine and so on. But with the free interchange of narcotic drugs as well as other products the people of Europe began to make use of cocaine and opium, and the highly potent distilled spirits of Europe were introduced to primitive races, where they began to supplant the mild fermented liquors they had been using for centuries. These fermented drinks of native origin have recently been shown in some cases to be the main source of necessary vitamins (notably the vitamin B complex) in an otherwise deficient diet, so that the change in type of alcohol used, or attempts to prohibit the local product, may cause the appearance of vitamin deficiency diseases as well as the harmful effects of the immoderate use of potent spirits.

In one respect these drugs of addiction resemble an infectious disease, in that their prolonged use by a people eventually leads to a decrease in the number of persons whose excessive consumption of the drug causes serious mental and physical deterioration, and instead the majority are found to be still using the drug, but in such moderation as not to give rise to serious symptoms. Examples illustrating this can be found almost everywhere, for instance in Europe drunkenness is almost unknown among the Mediterranean peoples who have been using wines for very prolonged periods, whereas in the more northern countries whose general use of alcohol is a more recent acquisition and whose inhabitants are inclined to drink the more potent distilled spirits more freely, as well as fermented

beverages, drunkenness is still all too frequent. Other examples arise to the mind such as that of the Sikhs in India who take their one or two opium pills a day and appear to derive benefit therefrom, but amongst whom excessive use of opium is of the rarest occurrence, and the aboriginal natives of South America make use of cocaine in the same way and benefit by its use, but never give way to its abuse. Then let us look at the other side of the picture and see the effect of the sudden introduction to races, of a type of narcotic to which they were not hitherto accustomed. The ravages of distilled spirits among the native races of Africa, North America and the South Sea Islands after their introduction by Europeans are well known, and cocaine and opium or its alkaloids claimed and still claim many more victims in Europe and other countries, into which they were introduced relatively recently, than they do in their countries of origin where they have been used for hundreds of years. To sum up this paragraph, narcotics appear to establish some kind of immunity or resistance to their abuse in races that have used them for a long time.

Consideration of these facts raises the question as to the best method of dealing with the drug menace. While there is no doubt that preventing the introduction of new narcotics into countries not accustomed to them is of prime importance, it is doubtful if the long view would not be preferable regarding the control of narcotics that have already been in use for centuries. By this we mean that limited official efforts at restriction with the hope of the eventual disappearance of the dangerous aspect of drug addiction would perhaps be preferable to the sudden stoppage of supplies in the attempt to stamp out completely and at once the use of a certain drug. The failure of prohibition in the United States of America with its tremendous

increase in crime and excesses of all kinds as secondary effects to the attempt to stop the use of alcohol altogether, as well as the rise in the clandestine consumption of poisonous trade spirit as a drink, is a striking indictment against this method of control. Another difficulty regarding the absolute prohibition of these drugs is that their cultivation and manufacture cannot be totally prohibited because large amounts are necessary for their legitimate use, the treatment and cure of disease.

Addicts to any drug can be treated, and often successfully, to overcome their craving. A striking example is the success of the lecithin and glucose treatment of opium addiction practised in recent years at the Calcutta School of Tropical Medicine. This is also a complicated problem, because although it is agreed that a great deal can be done in freeing a slave to the habit from the influence of a drug, it is now considered by those with experience in this matter that a large number are bound to relapse. Although such reasons as the example of companions, business worry, prolonged painful illness, etc., are given and accepted as explanations of beginning the habit, it is now stated that, in addition to one of these causes, there is an inherent weakness in the individual which is the basic cause of his subordinating his own initiative to the power of a drug. Even if he is relieved of this influence by treatment and the craving disappears for a time, the weakness is still there and is likely again to become manifest by a relapse into his former habit of excessive drug taking.

A short article of this kind is not the place for the discussion of preventive measures in detail as the problem is much too vast, so we have confined ourselves to the statement of a few aspects of the subject to indicate in some slight degree its complexity and difficulty.

## Special Articles

### USE OF HEMP DRUGS IN INDIA\*

By R. N. CHOPRA, C.I.E., M.A., M.D., SC.D. (Cantab.),  
F.R.C.P. (Lond.)

BREVET-COLONEL, I.M.S. (Retd.)

(From the School of Tropical Medicine, Calcutta)

#### Historical and General

*Introductory.*—The habitual use of drugs of a stimulative and restorative character was prevalent in India probably long before any of the other countries of the modern world. The juice of the Soma plant was a favourite drink of the Aryan settlers and was regularly taken by them many centuries before the Christian era. What

exactly was the Soma plant is not known, though a number of plants such as *Cannabis sativa*, *Ephedra vulgaris*, *Asclepias acida*, etc., have been implicated. During the Hindu period, i.e., up to the 8th or 9th century A.D., alcoholic beverages were used by the people as well as the preparations made from hemp drugs. These produced not only a sedative effect, but also brought about euphoria in the form of pleasant dreams, forgetfulness and, it would also appear from the writings of that period, voluptuous satisfaction. Opium and poppy were introduced on the west coast about the 9th century A.D. by the advent of the Mohammedan traders and opiates soon came into use. A study of the records shows that during the period of the Moghul Empire alcoholic beverages, opiates and hemp drugs were freely used. A

\* Being a lecture delivered at the Royal Asiatic Society of Bengal on the 29th of March 1940.



decoction made from poppy capsules known as 'koknar' was extensively used all over India. A beverage containing wine, opium, Indian hemp and poppy capsules, known as 'Chaharbargha' (four-leaved), was drunk by the well-to-do classes in the time of Akbar (1556 to 1605) and later. Opium on account of its stronger effects appears to have taken a great hold on the people, and poppy was extensively cultivated all over the country during this period and was indulged in by all classes.

The hemp drugs commonly used in India are derived from the flowers, fruits, leaves (and the resinous matter derived from the leaves), young twigs, and bark of the stem of the plant known as *Cannabis sativa* Linn. The plant belongs to the family *Cannabaceae* and has been found growing in a state of nature to the south of the Caspian Sea, in Siberia, in the desert of Kirghiz in Russian Turkestan, in Central and Southern Russia and along the southern lower slopes of the Caucasus mountains. In China, where probably it is indigenous on the lower mountain tracts, it has been known since the 6th century B.C. It grows in almost a wild state in Iran and in the Western Himalayas and Kashmir, and it extends to the east of Assam.

For some time the European form of the plant was supposed to be distinct from the Asiatic, the chief value of the latter consisting in its narcotic properties; but this distinction has now disappeared from the literature on the subject. *Cannabis indica* Lamk., the Indian plant, has thus been reduced to *C. sativa* Linn.

The hemp drugs are used in India in three principal forms, *ganja*, *charas*, and *bhanga*. *Ganja* is the female flowering tops and twigs covered with resinous exudation, *charas* is the resinous exudation found on the leaves, young twigs, bark of the stem, and even on the young fruits; *bhanga* is composed of the mature leaves and in some parts of India of the fruits also.

*Early historical references.* (a) *In Hindu medicine.*—Mention of hemp drugs is found in the classical literature as well as in the works on medicine of many countries old in the world. The plant is referred to in the ancient Sanskrit literature under the three names: 'bhanga', 'indracana' and 'vijaya' or 'jaya'. The earliest mention of the word 'bhanga' occurs in the Atharva Veda which, according to Western scholars, dates from 2000 to 1400 B.C.

The first mention of 'bhanga' as a medicine occurs in the works of Susruta (6th to 7th century A.D.) where it is described along with a number of other drugs as an antiphlegmatic. In the 10th century A.D., the intoxicating properties of the plant seem to have been already recognized. In the 14th century, the intoxicating properties of 'bhanga' were certainly well known as it is mentioned in some of the dramatic literature of that period.

In Sarangadhara Samhita, a medical work written about 1500 A.D., it is described as an excitant and is mentioned along with opium in the same passage. In the Bhavaprakash (about 1600 A.D.), a number of important properties of the hemp drugs are given with special stress on its digestive and stimulant effects on biliary secretions.

(b) *In Arabian and Persian medicine.*—Hemp is frequently mentioned in the early Arabic and Persian literature. The oldest work in which it is noticed is

a treatise by Hassan (658 A.D.). In the Arabian Nights, frequent references to hemp have been made under the old name 'benj'. The Arabic name 'benj' and the Persian name 'beng' are so closely related phonetically to the Sanskrit 'bhanga' that there is a strong presumption of their origin from the latter source.

(c) *In European literature.*—Hemp is also frequently mentioned in the early classical literature of Europe. The ancient Scythians seem to have been acquainted with the narcotic properties of the plant as well as with its fibre. They used to induce a state of excitement amongst themselves by inhaling its vapour. More recently, hemp was brought to the notice of European medicine through the accounts of Sylvestre-de-lacy in 1809 and Rouyer in 1810. These authors were attached to Napoleon's expeditionary forces in Egypt and during their stay there, collected a large amount of information regarding hemp drugs and published their findings and observations.

#### PRODUCTION OF HEMP DRUGS IN INDIA

(a) *Wild growth.*—As has been already stated, hemp grows wild over extensive tracts in northern India and along the slopes of the Himalayas. It is interesting to note that hemp seems to have the capacity for growing with equal luxuriance under almost any climatic conditions. With the change of climate, and the consequent alteration in the conditions of growth, however, some of the important characters of the plant are changed or modified. Thus, in Europe, hemp produces a valuable fibre, while showing little or no tendency to produce the narcotic principle, which in Asia constitutes its chief value. On the mountain tracts of upper India, hemp yields a fairly good fibre, but in Kashmir and Ladakh, its narcotic principles become much more predominant. When hemp is cultivated in the plains of India, the resin (*charas*) is not generally secreted but the young female flowers and shoots show a tendency to develop the narcotic principle (*ganja*) instead. In other parts of India again, the narcotic property is often not developed until the fruits are mature.

The plant grows wild throughout the Himalayas from Kashmir to the east of Assam at an altitude up to 10,000 feet above sea-level. It extends down the southern slopes of the mountains and from there into the Punjab and the Gangetic plain for a limited distance. It is found in the hill tracts of Assam whence it spreads to the mountainous tracts of East Bengal. The southern boundary of this area begins approximately at Peshawar and runs through the middle of the Punjab and the United Provinces, from where it follows the course of the Ganges. In this region, the plant propagates itself from self-sown seeds but it is possible that the growth on the lower slopes of the Himalayas and in the Terai is to a large extent accounted for by the aerial dissemination of seeds from the mountains. The plant appears to be very hardy once it is well established. The soil need not be rich, but it should be well drained and permeable.

(b) *Cultivation.*—Though hemp grows wild in many parts of India, it has to be properly

cultivated in order to obtain, for commercial purposes, its fibre or its narcotic principle as the case may be. For a good growth of hemp a rich soil as well as elaborate methods of cultivation are required.

*Present extent of hemp cultivation.*—The Indian Hemp Drug Commission (1893-1894) obtained statistics of the area under cultivation and found that after deducting the area under fibre cultivation (which yields little or no narcotic principle), the total area under cultivation for narcotic purposes did not exceed 6,000 acres. At present cultivation of hemp drugs for the production of ganja and bhang by the wholesale vendors is only permitted under licence and is considerably less than 2,000 acres.

The cultivation of the hemp plant for intoxicating purposes is absolutely prohibited in Assam, United Provinces, and in the minor provinces of Delhi, Baluchistan, Coorg and Ajmere-Merwara, while in some of the major provinces, it is permitted, for the production of ganja only, in limited areas and subject to careful restrictions. Thus, in the Bombay Presidency the cultivation is allowed in four villages of Nagar taluk in Ahmednagar district. In Bihar and Orissa, ganja is cultivated in Bhagalpore district. In the Madras Presidency, ganja is cultivated only in the village of Santaravur. In the Central Provinces and Berar, cultivation of the plant is restricted to a small area in Khandwa district. These areas are only able to meet the actual demand for their respective provinces. The main supply of ganja, however, comes from a place called Naogaon in the Rajshahi district of Bengal. This small area supplies ganja to the whole of the Bengal Presidency and also to other provinces, Indian States, and foreign territories where cultivation is prohibited.

If we compare the present figures with those published by the Indian Hemp Drug Commission in 1893-94, we are struck with the progressive decline of hemp-drug cultivation in India. For years together, the Government of India has followed a policy of gradually cutting down the area of hemp under cultivation and the total yearly outturn with the idea of reducing the hemp-drug addiction to a minimum. Hemp is not cultivated in this country for the production of charas and therefore these remarks do not apply to this form of the drug.

(c) *Manufacture of bhang, ganja and charas.*—Hemp drugs that are obtained by cultivation or from spontaneous growth require further treatment at the hands of experts before they are fit for consumption as narcotics.

1. *Manufacture of bhang* (synonyms 'siddhi', 'subzi', 'putti', 'sawi').—Bhang consists of specially dried leaves and flowering shoots of both female and male plants, wild or cultivated. The inclusion of male plants and male flower heads in the manufacture of bhang is not considered of special advantage as the male flowers are believed to contain very little of the active principle. Recent work has thrown doubt on this belief.

The narcotic principle in hemp develops only when the plant matures, reaching its maximum about the time of flowering and then it gradually begins to disappear when the leaves and the flowers turn yellow. Therefore, for the manufacture of good bhang, the leaves should be separated when they are just mature and when there are no signs of decay or withering. The usual time for gathering leaves varies in different localities but generally it is done during the months of May and June in the plains and during July and early August in the hills.

2. *Manufacture of ganja.*—Ganja ['ganja yala' (Tamil) and 'bhangaku' (Telugu)] consists of dried flowering tops of the cultivated hemp plant which become coated with a resinous exudation, chiefly from the glandular hairs, in consequence of being deprived

of the opportunity of setting seeds. To secure these results, the male plants are removed from the field at an early date. As the female plants begin to form ganja, all the large leaves on the stem and branches are also removed. The smaller leaves and the brackets of inflorescence become agglutinated into a mass called ganja. Fresh excise ganja has a rusty green colour with a characteristic odour. The colour and the smell are considered to be features of merit but as a rule ganja which has least mixture of leaf is regarded as the best. The plants thus collected require further treatment to form the ganja of commerce sold by the excise vendors. In Bengal the entire plant is cut, while in Bombay the flowering tops are generally pulled off by hand.

3. *Manufacture of charas.*—Charas is the name given to the resinous matter collected from the leaves and flowering tops of the plant and constitutes the active principle of hemp. Charas, as sold in this country, is a greenish mass, with a peculiar and characteristic odour. When kept for some time, it becomes hard and friable and acquires a brownish-grey colour, thereby losing most of its narcotic properties.

Although the hemp plant, when cultivated in tropical countries such as India, Africa and Malaya, becomes rich in narcotic principles, it seldom yields enough resin to be collected as charas. On the plateaux of Central Asia and southern Himalayas (Nepal) charas is sometimes collected, but it is poor both in quality and yield. The best quality and the maximum amount of resin is obtained from plants grown in Yarkand in Chinese Turkestan in Central Asia.

*Manufacture of charas in Chinese Turkestan.*—In Chinese Turkestan at an altitude of 3,000 to 5,000 feet above sea-level, *Cannabis sativa* grows extensively in a state of nature. It is also cultivated along with other field crops. The plant flourishes well in these plateaux often attaining a height of 8 to 10 feet. It matures during the month of September or October when big tufts of flowers appear at the top of each plant, which can be collected and used in the preparation of finished charas. The method of charas manufacture in these areas is entirely different from that in use in India. The female flower heads are first dried, then broken and crushed between the hands into a powder, which is passed through sieves so that it attains the fineness and consistency of sand or saw dust. This powder, which is still green, is stored in bags made of raw hide for four or five months during the winter. With the onset of the hot weather the material is taken out and exposed to the sun for a short time, sufficient to allow the resin to melt. It is stored again in hide bags of 10 lb. to 14 lb. capacity. After a few days, the agglutinated mass is again taken out and kneaded well by means of wooden rods so that a certain amount of oily matter appears on its surface. The process of kneading is repeated till each bag yields about one to two lb. of oil. At this stage charas is transferred into fresh hide bags and is ready for sale and distribution.

*Trade and traffic in charas.*—Charas forms one of the most important articles of trade between Central Asia and India. It is usually brought down from Yarkand in the month of August when the mountain passes are opened and it reaches Leh in Kashmir by September or October. The payment for charas is usually made in kind and not in currency. All forms of piece-goods which are apparently in great demand in Central Asia are generally accepted as barter.

The traffic in charas has always been carefully regulated by the Punjab Government; the charas bundles are checked at Panamik and again at Leh in Kashmir State to ensure that any bundle which reached Leh (where the Punjab Government has established a warehouse and maintains a special staff) was again accounted for either in Kashmir State or in one of the Punjab warehouses. Each bundle of charas, which ordinarily weighs about 50 seers (100 lb.), is recorded in Leh and forwarded either to Kulu or to Rawalpindi, or is consumed locally under the control of Kashmir State authorities in the State. There are four warehouses in the Punjab, at Sultanpur (in Kulu),

Hoshiarpur, Amritsar, and Rawalpindi. The Government of Chinese Turkestan have now totally stopped the import of charas into India.

*Illicit traffic in charas and measures to combat it.*—Contraband charas comes into India nowadays mostly through Chitral and to a certain extent through independent tribal territories. It is also brought across the Indus river principally to the neighbourhood of Peshawar. The drug is mainly smuggled by travellers who carry small quantities at a time upon their persons. Very often it is said to be exchanged for smuggled cocaine from Calcutta and other parts. In fact, it has been stated that the practice of charas smuggling in the Punjab and the North-West Frontier Province has been responsible for the introduction of the cocaine habit in those areas.

In parts of India where the consumption of the drug is totally prohibited, there is reason to believe that illicit charas is still being sold to a certain extent. In other parts where the consumption is permitted but the duty is high our inquiries reveal that smuggling is far from being checked and the drug is frequently obtainable through illicit sources.

#### THE NARCOTIC PRINCIPLES OF HEMP DRUGS

An interesting feature about the formation and development of the narcotic principle is that this process is generally found to be associated, and sometimes runs parallel with some distinct morphological modification of the plant anatomy. In some plants, the leaves are the chief organs where the narcotic resin is found; in others, the flowering tops assume the important rôle of storing and secreting the resin; while in a third group, the fruits and the surfaces of stems take upon themselves the secretory function. The first group of plants where the narcotic is primarily stored in the leaves yields the bhang of commerce, the second group affords ganja, and third group is considered particularly suitable for the production of charas. The factor or factors which are responsible for such modifications in the physiology of the hemp plant are not known.

The resinous substance contained in hemp is considered the most important principle responsible for the physiological activity of the drug. The resin as obtained from the plant apparently contains a number of compounds, one of which is *cannabinol* (Cahn) and which is probably the active principle. There is no satisfactory evidence to show that the other constituents are physiologically active.

*Deterioration of the narcotic principle.*—The narcotic principle of the hemp drugs deteriorates with age, though it is difficult to give the precise period during which a preparation can retain its activity under ordinary conditions of storage. The popular impression is that hemp drugs retain their activity for a period of at least two years without appreciable loss. Some authorities consider that the potency remains intact for a much longer period. The experience of the excise authorities in the plains of India is that ganja retains most of its activity for one year and during the second year it begins gradually to lose its potency until it becomes quite useless and unsaleable at the end of two years. It must be realized, however, that the retention of physiological activity of the three different types of hemp drugs, like that of many other medicinal products, largely depends on the climate and also on the care exercised during its storage. Bhang is not as susceptible to deterioration as ganja and may keep in fairly good condition for three to four years, if not

directly exposed to sun and air. This comparatively slow deterioration of bhang is supported to a certain extent by the subjective symptoms complained of by the bhang addicts.

With regard to the keeping properties of charas, it is still more difficult to make any definite statements. However, the general opinion of dealers in this drug is that charas is very potent during the first year, after which it gradually loses its activity until the fourth year, when it becomes practically inert and useless.

#### MODES OF CONSUMPTION

Ganja and charas are mostly smoked, while bhang is taken by the mouth in the form of a beverage or a confection. The latter method, eating of hemp for narcotic purposes, would appear to be a much older method of indulgence than smoking.

1. *Hemp drinking and eating.*—The beverage made from bhang is known by different names in different parts of India. It is called 'thandai', 'siddhi', 'sardai', 'sawi', and 'sukha' in the Punjab and United Provinces; in Bombay and Central Provinces, it is known as 'bhanga' or 'ghota' or 'pang'; in Bengal, it is called 'siddhi'; in Rajputana and Central India, 'dudhii'; in South India hemp beverages are known as 'ramras' or 'ram-rasam' and correspond to 'dudhii' and 'siddhi' of upper India.

The simplest form of consumption consists of a drink made from bhang leaves by pounding them together with a little black pepper and sugar and adding enough water to reach the desired strength. Various kinds of special beverages are prepared by the middle and well-to-do classes by the addition of almond kernels, sugar, iced milk, curds, etc. A number of other ingredients are at times added to improve the taste and possibly with the idea of enhancing the euphoric effects produced by these drugs. Amongst these, aniseed, ajowan, cucumber, melon and poppy seeds, rose petals, saffron, cloves, cardamoms, musk and essence of rose are the most common. Besides their common use as a beverage, bhang leaves are sometimes chewed for their sedative effects. This is done at times when it is not convenient for the individual to prepare the beverage, for instance during travelling, and also during the winter season when the system does not require large quantities of fluid.

A number of preparations containing bhang are made in different parts of India. Sweetmeats containing bhang are sold and even ice cream containing powdered leaves is available in some towns.

2. *Hemp smoking.*—Ganja and charas are usually consumed by smoking. Different kinds of apparatus have been improvised in various parts of the country for smoking hemp drugs, the one commonly used being an earthenware 'chillum' (used for smoking tobacco) with an elongated neck. The ordinary 'chillum' used for smoking ganja and charas resembles a funnel with a long neck and a somewhat wide base.

The method of smoking is simple. Ganja is first moistened with a little water to render it soft. The mass is then kneaded till it changes to a pulpy mass. A small amount of tobacco (almost equal in amount to the ganja taken) is then placed in the 'chillum' and the 'prepared ganja' is placed on the top of it. The usual practice is to place the prepared mass of ganja (or charas as the case may be) between two thin pieces of broken earthenware pottery. After the 'chillum' is prepared, a piece of glowing charcoal or a piece of

smouldering cow-dung cake is placed in it. The smoke is inhaled into the lungs by powerful inspiratory efforts and the narcotic principles are at once taken into the blood. The smoke is retained in the lungs as long as possible and is then allowed to escape slowly through the nostrils, the mouth being kept shut. The longer the smoke is retained inside the lungs the better the effects obtained. Apart from the 'chillum' method just described ganja and charas are also smoked by the ordinary 'hooka', the smoke being allowed to pass through water before it is inhaled. This is the common method employed in the north-western districts of the Punjab and the North-West Frontier Province, but it has not become popular in other provinces in India where smoking of hemp drugs is prevalent. Recently, cigarettes containing bhang have been used in certain towns. Both bhang and charas are occasionally smoked in an ordinary tobacco pipe, but this method has not become very popular.

Unlike opium smoking, which is indulged in by the smoker alone and away from his friends, hemp smoking is always preferred and enjoyed in the company of others. The smokers, usually two to five in number, sit down in a small circle and the prepared 'chillum' is passed round from one to the other so that each can take two or three deep pulls at it. Ganja or charas worth at least four to six pice (1 or 1½ penny) is required for preparing a full 'chillum'. The quantity of hemp procurable at this price is usually sufficient to produce narcotic effects of a mild degree on three to five persons.

Charas is smoked more or less in the same way as ganja but there is some difference in the initial preparation of the drug. Charas is usually warmed a little in the early stages and is mixed with approximately double its quantity of tobacco before being put in the 'chillum'. Charas is generally considered to be a stronger preparation and, therefore, a smaller quantity of the drug is used.

Besides ganja and charas, bhang leaves are also smoked at times. 'Sirkali' or the flowering tops of the hemp plant are sometimes cut and dried and smoked in a 'chillum' alone or mixed with tobacco.

#### USES OF HEMP DRUGS IN INDIA

Hemp drugs have been used in India from very early times in order to overcome fatigue and worry, for production of euphoria, and to give courage to warriors during times of stress. The present use of these drugs may be conveniently considered under three main headings:

(i) use in connection with religious and social customs, (ii) medicinal uses, and (iii) employment for narcotic and euphoric purposes.

(i) *Uses in connection with religious and social customs.*—The use of hemp drugs in connection with religious and social practices is still met with in almost all the provinces of India, though to a much smaller extent than in the past.

In Bengal, for instance, the custom of offering a beverage prepared from the leaves of the hemp plant to the members of the family and to the guests present on the last day of the Durga Puja (Bijaya Dasami) still persists. In Tarakeshwar Temple in Bengal ganja is used as an offering on the Shivaratri (Shiva's night). Less commonly, it is used in other religious festivals such as Trinath Puja, a religious ceremony observed also by certain Mohammedan sects in slightly different form. In Puri (Orissa) ganja and bhang are largely used by the attendants and worshippers of Jagannath. In the United Provinces where Durga Puja is observed in a manner similar to that in Bengal, the use of bhang is not so much in vogue. It is, however, taken by certain classes on the occasion of the Holi and Dewali festivals, marriage ceremonies

and other family festivities. Among the Sikhs, the use of bhang as a beverage was quite common 20 or 30 years ago and these beverages were freely distributed to devotees attending some of their religious places and shrines. Drinking of bhang is also in vogue in Rajputana at the festival of Kama (Indian cupid) by the Rajputs of Bondil. In the Central Provinces 'ghota' is used among the lower classes at the time of different festivals. In Bombay, worshippers of Shiva generally use ganja, while the Marwaris and merchant classes who belong to religious sects such as Jains use bhang on festive occasions. In Madras, the use of hemp drugs in religious and social life is less common than in other provinces. Assam is the only province where bhang is used practically not at all at the present time, probably because of the prevalence of the use of opium in that province.

It may be pointed out that charas, which is a foreign product and which has been comparatively recently introduced into India, is not in any way connected with religious worship or observances.

From the foregoing description it is evident that the use of hemp drugs in social and religious customs is still in vogue though it has considerably decreased during the last two or three decades. Even to-day a religious mendicant smoking ganja is not only tolerated but is looked upon with some veneration and is even considered to possess supernatural powers of healing disease and infirmities, by some of the illiterate classes. Sects of 'sanyasis', 'mahantas', 'mantra-data gurus' or religious preceptors are held in great respect although they indulge freely in hemp drugs. In fact, offering of hemp to them is considered to be an act of piety.

(ii) *Medicinal uses.* (a) *Indian hemp in Hindu medicine.*—In the Ayurvedic medicine, the first mention of the hemp plant occurs in the work of Susruta written before the 8th century A.D. In this work hemp leaves are recommended along with a number of other drugs as antiphlegmatic, as a remedy for catarrh accompanied with diarrhoea and as a cure for fever arising from excess of 'bile' and 'phlegm'. The hemp plant was believed by the ancient Aryans to possess cooling and febrifuge properties. On account of its narcotic properties it was probably also used as an anæsthetic by the ancient Indian and Chinese surgeons.

(b) *Indian hemp in Mohammedan or Unani medicine.*—Rumphius (1095 A.D.) in the *Herbarium amboinense* states that the Mohammedans frequently used the male hemp plant in the treatment of gonorrhoea, asthma, and also in the treatment of a condition, popularly called 'stitch in the side'. He also adds that the powdered hemp leaves are stomachic and check diarrhoea and excessive biliary secretion. He mentions the use of hemp as an enema in strangulated hernia, and as an antidote in poisoning with orpiment. In *Makhzanul aldawaiya*, the well-known Arabic book on materia medica, the author dwells on the wonderful properties of the hemp plant. It is said to be a cordial, a bile absorber, an appetizer, and that its moderate use prolongs life. The powdered bark is recommended as an external application to fresh wounds and sores. A poultice made by boiling the roots and leaves of the hemp plant is prescribed for application to inflamed parts as a cure for erysipelas and for allaying neuralgic pains. The oil expressed from the hemp seeds is known as 'kandiryak' and is used in Kashmir as well as in certain parts of the Punjab as an application for rheumatic pains.

(c) *Indian hemp in western medicine.*—The introduction of Indian hemp into western medicine may be traced back to the period when Napoleon's expeditionary forces occupied Egypt. In India, O'Shaughnessy in 1839 tried Indian hemp as a sedative of the central



nervous system in such diseases as tetanus, hydrophobia, rheumatism, chorea, and convulsions in children. Christison also carried out clinical trials in Indian patients and considered it to be an anodyne, hypnotic, and antispasmodic next only to opium. Later, Aaronson used it on some of his patients undergoing surgical operations and they testified that the drug subsequently had some pain-relieving properties. During the period that followed the report of these early workers, Indian hemp was used for its analgesic and hypnotic properties in such affections as asthma, neuralgia, neuritis, migraine, sciatica, myodynia, gastrodynia, enteralgia, tinnitus, dysmenorrhoea, muscular and joint pains, etc. It was also used to relieve the lightning pains of tabes, fornication, numbness, paresthesia, convulsions, etc. On account of its diuretic and sedative properties a decoction of hemp leaves has also been used in cystitis and urethritis.

(d) *Indian hemp in veterinary medicine.*—For diseases of cattle, hemp leaves are frequently used mixed with such ingredients as spices, salt or sugar candy. The smoke produced by the burning hemp plant is considered to be a disinfectant for sheep folds. Ganja is considered to be a good remedy against intestinal worms and in 'foot sore' disease. Bhang is sometimes used to increase the flow of milk in cows. Bhang mixed with salt is often administered to cattle as a preventive against diarrhoea, which is of common occurrence in India during the mousoon months. The use of these drugs is chiefly based on hearsay and tradition.

(e) *Indian hemp as a household remedy.*—The hemp drugs are popularly used as household remedies in the amelioration of many minor ailments. A mild beverage made from bhang leaves is believed to sharpen appetite and help digestion. Indian hemp is commonly used as a smoke and as a drink for its supposed prophylactic value against malaria in malarious tracts. Bhang beverages form one of the popular household remedies for gonorrhoea and dysuria. On account of their mild diuretic and sedative properties these drinks probably give a certain amount of symptomatic relief. Likewise, the use of bhang in dysmenorrhoea, asthma, and other spasmodic conditions is not uncommon. A poultice made from fresh leaves is a common household remedy for painful affections of the eyes, conjunctivitis, swollen joints, orchitis, and other acute inflammatory conditions.

(iii) *Use of hemp for euphoric, intoxicating and aphrodisiac purposes.*—The habitual use of hemp drugs for the production of euphoria and intoxication is widespread not only in India but throughout Asia and Africa. According to reports in published literature, it is a fairly common habit in the southern states of the United States of America where it is generally known as 'marihuana'. The rapid development of its use since 1935–1936 and widespread traffic in it has been the source of very great concern to the Bureau of Narcotics. Particularly disturbing is the fact that the victims comprise for the most part members of the younger generations and even boys and girls of school age are not excepted.

These drugs are said to alleviate fatigue and also to increase the 'staying power' in severe physical stress. In India, fishermen, boatmen, washermen, and cultivators who have to spend long hours of the day in rivers, tanks and water-logged fields often resort to hemp drugs in some form or other in the belief that these will give them a certain amount of protection against catching cold. Mendicants who roam about aimlessly in different parts of India and pilgrims who have to do long marches often use hemp drugs habitually. Sadhus and fakirs visiting religious shrines usually carry some bhang or ganja with them and often indulge in them. It is not an uncommon sight to see them sitting in a circle and enjoying a smoke of ganja in the vicinity of a temple or a mosque. Labourers who have to do hard physical work use hemp drugs in small quantities to alleviate the sense of fatigue, depression and sometimes hunger. A common practice amongst labourers engaged on building or excavation work is to have a few pulls at a ganja pipe or to drink

a glass of bhang towards the evening. This produces a sense of well-being, relieves fatigue, stimulates the appetite, and induces a feeling of mild stimulation, which enables the worker to bear the strain and perhaps the monotony of his daily routine of life more cheerfully. The low cost and easy availability of these drugs are important factors in their use by the working classes, whose economic condition is low in this country. Hemp drugs are perhaps the only narcotic drugs which fall comfortably within their means and they make use of them as occasion arises. A dose worth two to four pice ( $\frac{1}{2}$  to 1 penny) is often sufficient for producing the desired effect in a few individuals.

Hemp drugs are also sometimes used to induce a state of intoxication which will excite emotion and give a sense of bravado so that daring acts may be committed. As has been said the Rajput warriors, during their frequent encounters with the Mohammedan invaders in the old days, used to indulge in bhang so that any nervousness present might be banished, and a feeling of determination created either to win or die on the field of battle. This practice is seen even in these days in connection with wrestling contests and athletic sports and games needing great physical effort and endurance. Indulgence in hemp drugs, unlike alcohol, rarely brings the habitué into a state of extreme intoxication where he loses entire control over himself. As a rule, the intoxication produced is of a mild nature and those who indulge habitually can carry on their ordinary vocations for long periods and do not become a burden to society or even a social nuisance.

Another purpose for which hemp drugs are largely used in this country is for their aphrodisiac effect. The belief regarding their stimulant effects on the sexual organs has been in existence for a very long time. According to the physiological data obtained it is possible that hemp drugs by their action on the higher centres of the brain, may excite ideas and delusions of a sexual nature, but no experimental data are available to show that they have any specific action on the lower sexual centres in the cord or directly on the organs.

The use of hemp drugs for euphoric, intoxicant, and aphrodisiac purposes, although quite common 20 to 30 years ago, has gradually declined and at the present time it is almost entirely confined to the lower strata of society. Amongst the upper and middle classes, the use of hemp drugs is nowadays considered to be derogatory, in spite of the fact that the practice was held in great esteem in ancient India, and early literature is full of references to the virtues of this drug.

This change in outlook with regard to indulgence in them is not difficult to understand. One reason is that hemp drugs are popular with the lower strata of society which contain a large number of undesirable and criminal elements, and the well-to-do and respectable classes are giving them up on account of this association. Another and perhaps a more important reason for the decline of the use of hemp drugs is probably traceable to the peculiar blunting of the sense of relativity in which the idea of time and space may be lost. By affecting the higher nervous pathways concerned in the balanced co-ordination of time and space, the use of Indian hemp, unlike other drugs which produce euphoria, is more likely to place the habitué in an awkward position and bring him into ridicule. Behaviour problems are also known to arise commonly with them. These lapses naturally become immediately apparent in social and club life and make the company of such persons undesirable. The upper and middle classes, therefore, abstain from the use of these drugs as far as possible. Whatever may be the reasons for the decline in the use of hemp drugs, statistical data undoubtedly show a marked decrease in their consumption during recent years, especially among the upper classes.

#### ABUSES OF HEMP DRUGS

The hemp drugs are rarely employed to produce a state of intoxication which is so intense that the

individual may lose all control over himself. Although their habitual use is common, these drugs are not often indulged in to such an extent as to constitute a definite abuse. The deliberate abuse of bhang is met with among certain classes of religious mendicants in this country, their main purpose being to get into a state of frenzy which, according to their traditional ideas, is conducive to mental concentration and communion with God. Such a frenzied state is used as a cloak for creating belief in the minds of the credulous illiterate masses. A large number of religious fanatics in temples and in places of pilgrimage undoubtedly are hemp-drug addicts of long standing.

Another class of people who are prone to abuse hemp drugs are some of the nomadic classes who have no fixed home and who move about from place to place living in small camps by the roadside exposed to all sorts of inclement weather.

It is commonly believed that bhang drinking is comparatively less harmful than the practice of smoking ganja and charas. There appears to be a good deal of truth in this popular belief. Although the use of bhang as a cooling beverage is encountered in many parts of India and cases of excessive indulgence are not frequently met with, instances of frank abuse and harmful effects following therefrom are as a rule uncommon. This, of course, does not mean that bhang does not produce any deleterious effects on the system. Impairment of digestion is a common occurrence with bhang drinkers of long standing, who take excessive quantities. This naturally results in injury to their general health and vitality. There is definite and demonstrable stimulation of the higher cerebral and medullary centres, but this is seldom intense and, therefore, the harm done is comparatively small. The smoking of ganja and charas on the other hand, although it affects the digestion to a lesser extent, brings about a state of intense intoxication as a result of action on the higher centres in the brain and, if the abuse is continued for a considerable time, it may lead to mental derangement, behaviour problems, crime and insanity. These habits, therefore, constitute an important social problem. Moreover, ganja and charas are possibly more likely to produce intense addiction than bhang. Habitual use of bhang can be discontinued without much trouble but the withdrawal from the ganja and charas habits is accompanied by unpleasant symptoms and is much more difficult, though negligible compared to those associated with drugs like opium or cocaine.

#### PRESENT EXTENT OF HEMP-DRUG ADDICTION

*Total consumption of hemp drugs.*—The total consumption of hemp drugs, according to excise returns of 1934-35, amounted to 1,031,496 lb. in British India and this works out approximately at 4.24 lb. per 1,000 of population per annum (census of 1931). The consumption of these drugs in British India in 1912-13 worked out at 15 lb. per 1,000 of population per annum. It will be seen therefore that, during the last 20 years, the use of these drugs has been reduced to nearly a quarter of what it was. When the three preparations, bhang, ganja, and charas, are considered individually, the amounts consumed in 1934-35 were as follows:—

		Seers or	lb.
Bhang	..	292,166	584,332
Ganja	..	162,153	324,306
Charas	..	61,429	122,858
TOTALS	..	515,748	1,031,496

The United Provinces consume the largest amount of hemp drugs, the total consumption in that province being 287,926 lb. during 1934-35; next in order come the Punjab, Bengal, Bombay, and Central Provinces.

As regards the incidence of the hemp-drug habit,

Sindh shows the highest incidence with a consumption of 35.12 lb. per 1,000 of population per annum, then comes Delhi with 23.84 lb., Ajmere-Merwara 14.6 lb., Baluchistan 8.22 lb., the Punjab 7.6 lb., North-West Frontier Province 5.94 lb., United Provinces 5.94 lb., Bombay 4.4 lb., Assam 2.18 lb., Bihar and Orissa 2.2 lb., Bengal 1.6 lb., and Central Provinces and Berar 1.6 lb., respectively.

It is very difficult to form an accurate idea of the number of persons addicted to the three forms of hemp drugs as there are many occasional consumers, and there is no system of registration of addicts. It is only possible therefore to form a very rough estimate of the number of addicts from the total amount of the three preparations consumed and the average dose taken.

The average daily dose of bhang, ganja, and charas has been carefully worked out by us in more than 1,500 addicts. This is approximately as follows:—

	Grains daily
Bhang .. ..	20
Ganja .. ..	18
Charas .. ..	15

Assuming that the whole amount was used for euphoric purposes and for habitual consumption (the amount used for medicinal purposes being negligible), the number of hemp-drug addicts in the whole of British India at the present time works out to be 855,844, provided only the amount issued by the excise authorities is considered. From the knowledge we have of the situation all over the country, we are inclined to believe that the actual amount is a good deal higher, as considerable amounts of the drugs are obtained from illicit sources, for example by smuggling or from the spontaneous growth, which can be easily utilized.

The hemp drugs are the narcotics most extensively employed by the poorer classes throughout the country because they are cheap and easily available. Extensive work in the field has enabled us to estimate that the incidence of hemp-drug addiction ranges between 0.5 and 1.0 per cent of the total population in British India. The largest number of addicts are in the United Provinces and next comes Sindh. In these areas the use of hemp drugs is not restricted to any particular community and extends even among the middle classes. Charas is not used in Madras, Assam, Bihar and Orissa, and Central Provinces excepting in a few industrial towns such as Ahmedabad and Jubbulpur. Ganja is used to a comparatively small extent in Sindh, eastern districts of the United Provinces and in N.-W. F. Province and Punjab where it is prohibited.

From our investigations in the field, we conclude that a large number of the inhabitants of this vast country take hemp drugs habitually at the present time, that the habit is on the whole declining and it certainly is not on the increase anywhere, that there is reason to believe that during the last 15 years the use of hemp drugs has more rapidly declined than in the previous similar period; the cause of this decline appears to be the tightening of control by government by reducing the area under cultivation and increasing the price by enhancement of excise duty.

The localities in each province where the incidence of hemp-drug addiction is high are urban and not rural areas. Large industrial towns or large agricultural centres, as a rule, have large labour populations in low economic circumstances. They have to work very hard and they usually indulge in these drugs as cheap euphorics. Thus, in towns such as Calcutta, Bombay, Madras, Ahmedabad, Cawnpore, the consumption is high on account of this large industrial population. The mining areas also show a high incidence, due to the preponderance of labour forces. Burdwan district in Bengal with its large mining industries shows a comparatively higher incidence than other parts of Bengal, with the exception of Calcutta.

Religious centres and important places of pilgrimage also show a high incidence of the use of hemp drugs. This is due to the presence of hordes of mendicants who collect at such places.



## HEMP-DRUG ADDICTION IN DIFFERENT PROVINCES IN INDIA

**Bengal.**—During 1936-37 the consumption of different forms of hemp drugs in Bengal, according to the Excise Reports, was as follows: ganja 64,974 lb., bhang 16,736 lb., and charas 1,452 lb.

The incidence of the use of different forms of hemp drugs is high chiefly in the western zone, composed of Iwan, Birbhum, Midnapore, and

The high consumption in these to large labour forces engaged in various industries such as jute and cotton mills, iron and steel works, coal fields, etc., which abound in this area.

In most of the districts of East Bengal, the demand for bhang as an intoxicant is very small, but it should be remembered that in these districts bhang grows wild, and it is believed to be extensively used as an illicit substitute for ganja. Further, it will be seen that the consumption is highest in Calcutta and its suburbs. The reason of this is that in the city of Calcutta and its suburbs there is a large labour population engaged in different industrial occupations, whose hygienic and economic conditions are such as to lead to the use and abuse of narcotic and euphoric drugs.

Taking the Presidency as a whole the incidence of the use of these drugs is not very high, being only 1.6 lb. per 1,000 of population per annum for all hemp drugs and 1.4 lb., 0.4 lb., and 0.02 lb., for ganja, bhang, and charas, separately. There is no doubt that there is a further decline in these figures.

**Bihar and Orissa.**—In 1936-37, 57,726 lb. of ganja and 14,470 lb. of bhang were consumed in Bihar. Minor rises occur in the consumption of bhang in the districts of Gaya and Patna, in all probability because of their having places of pilgrimage to which people from other parts of India come in large numbers. The consumption of ganja keeps at a fairly high level throughout the province. The incidence of consumption of total hemp drugs per 1,000 population was 2.2 lb. per annum.

The types of people who use hemp drugs in these provinces are similar to those in Bengal, the only difference being that the incidence of addiction among the middle classes is higher than that in Bengal, particularly in the western districts which adjoin the United Provinces.

**Assam.**—Cultivation of hemp drugs is not allowed in this province, the supply of ganja being obtained from Rajshahi in Bengal and of bhang from Bhagalpore in Bihar. The amount of ganja consumed in Assam during the year 1935-36 amounted to 20,245 lb. The incidence per 1,000 population works out to be 2.2 lb. The consumption appears to have increased during the last year throughout the province except in Cachar, Sylhet, the Khasi Hills, Jaintia Hills, and the Garo Hills.

The consumption of bhang amounted to 60 lb. during 1935-36 which is very small as compared with other provinces. There are only two bhang shops, one in Cachar and another in Sylhet, but the consumption from excise sources is gradually decreasing, due to smuggling from Manipur and the Naga Hills. Permits are also issued to 47 druggists and Kavirajas who are allowed to store the drug for medicinal purposes. Those addicted to hemp drugs are mostly working class coolies and labourers.

**United Provinces of Agra and Oudh.**—The total consumption of all these drugs in the United Provinces was 287,942 lb. during 1934-35. Of this amount 228,724 lb. was bhang, 42,752 lb. charas, and 16,466 lb. ganja. As regards the incidence per 1,000 population per annum is concerned, it works out to be 5.8 lb. of all hemp drugs and 5 lb., 1 lb., and 0.4 lb. for bhang, charas, and ganja, separately.

**Punjab.**—Only bhang and charas are used in the Punjab, the sale of ganja being strictly prohibited. Total consumption of hemp drugs in this province during 1935-36 amounted to 179,408 lb. out of which 34,502 lb. was charas and 144,906 lb. was bhang.

The total incidence for the two drugs worked out at 7.6 lb. per 1,000 of population per annum and 1.4 lb. and 6.0 lb. for charas and bhang separately.

**Delhi province.**—As this province adjoins the Punjab and western districts of the United Provinces, the problem of hemp-drug addiction is very similar to these provinces. Bhang and charas are almost entirely used and the supply is obtained from the Punjab. Total consumption of these drugs during 1934-35 was 15,130 lb. out of which 5,702 was charas and 9,428 was bhang. The average consumption per 1,000 population per annum works out at 23.8 lb. and the province stands second in India with regard to the incidence of consumption.

**North-West Frontier Province.**—The problem of hemp-drug addiction in this province is similar to that in the adjoining provinces of the Punjab and Sindh. Bhang and charas are the only two preparations which are used in this province for addiction purposes. Indian hemp grows spontaneously almost everywhere and can be collected without restriction up to the legal limit of 2 lb. per person. During 1935-36, 6,768 lb. of charas were consumed in this province which gives the incidence of 4.2 lb. per 1,000 population per annum. The drug is used by all classes, who are chiefly Mohammedans.

Bhang is mainly consumed in Bannu and Dera Ismail Khan districts. This is probably because these areas lie on the border of western Punjab districts and Sindh which are both heavy bhang-consuming areas. The total consumption of bhang during the year 1935-36 was 12,242 lb. which gives an incidence of 1 lb. per 1,000 population per annum. The incidence of both forms worked out at 5.2 lb. per 1,000 population.

**Sindh.**—During 1934-35, 136,480 lb. of hemp drugs were consumed of which 118,660 lb. was bhang, 17,504 lb. charas, and 316 lb. ganja. The consumption of bhang is rather high throughout the province, and works out at 35.12 lb. per 1,000 population per annum.

**Baluchistan.**—The total consumption of hemp drugs during 1935 amounted to 3,352 lb., of which 2,164 lb. was charas, 1,186 lb. bhang, and only 2 lb. ganja. The average consumption of all the hemp drugs put together was 8.2 lb. per 1,000 of population per annum.

**Bombay Presidency.**—The total consumption of hemp drugs in the Bombay Presidency proper during the year 1936-37 was 79,646 lb., of which 16,214 were bhang, 12,476 lb. charas and 50,956 lb. ganja. Ganja is however the drug of choice, bhang is in little demand and is only used by the Marwari community and people from northern India. The use of charas is prohibited all over the province except in the towns of Bombay and Ahmedabad.

In this province, taken as a whole, it has been roughly estimated that about 1 per cent of the population use hemp drugs habitually in some form or other at the present time. The incidence of all drugs works out approximately to 4.4 lb. per 1,000 of population per annum. That for ganja, bhang, and charas is 8.4 lb., 2.8 lb., and 0.8 lb., respectively. There appears to be no doubt that, on the whole, habitual indulgence has considerably declined during recent years.

**Central Provinces and Berar.**—The total consumption of hemp drugs in this province works out at 1.6 lb. per 1,000 population per annum and that of bhang and ganja to 1.2 lb., and 2 lb.

**Coorg.**—The amount of ganja consumed during 1935-36 was 318 lb. and the incidence of hemp-drug addiction worked out at 1.8 lb. per 1,000 population per annum.

**Madras Presidency.**—The population of southern Madras uses hemp drugs to a lesser extent than that of northern parts. During 1934-35 the total consumption of ganja and bhang amounted to 89,172 lb., out of which only 12,158 lb. was bhang, the rest being ganja. The total average consumption amounted to 1.8 lb. per 1,000 population per annum. The incidence is somewhat high in Madras and Salem districts, in the former on account of its being an industrial centre and in the latter because it is a rich agricultural centre. The consumption of both ganja and bhang is low in all other districts. The use of charas is practically unknown. There are altogether 544 licensed shops in the presidency.

### EFFECT OF HEMP-DRUG ADDICTION ON GENERAL HEALTH

From an analysis of the statements of addicts (1,238) as to whether the general health is affected in any way, we have observed that in about 52.10 per cent no ill effects were admitted. In 24.47 per cent health was believed to be affected to a minor degree and in 14.78 per cent to a marked degree. There were, on the other hand, 8.64 per cent who stated that they had improved in their general health since they took to indulgence in hemp drugs. The last group of persons were mostly those addicted to the use of bhang and who were in the habit of taking small doses in the neighbourhood of 10 grains a day. It is also evident that the evil effects were admitted more frequently in the case of ganja and charas addicts than in the case of bhang addicts, in 65.02 per cent as compared with 23.7 per cent, in this series. Further analysis showed that with increased dosage, the adverse effects were admitted to be more pronounced.

It will thus be seen that the general health may not suffer when hemp drugs are consumed in doses below 20 grains daily; further increase in the dosage is attended with deleterious effects and consumption exceeding 180 grains a day may damage the health seriously and rapidly.

#### *Physical effects*

Moderate habitual use of ganja or charas may or may not be attended with harmful effects, and in the case of bhang there is evidence that no apparent harm may result if it is taken in moderate quantities. Of all the preparations of Indian hemp, bhang is popularly believed to be the least harmful. According to the Indian Hemp Drug Commission (1893-1894) it is the refreshing beverage of the people, corresponding to beer in England and moderate indulgence in it is attended with less injurious consequences than similar consumption of alcohol in Europe. This view has been corroborated by our own experience in the field.

Bhang drinkers, unlike other drug addicts, are robust and physically well-built individuals. Its moderate habitual use does not lead to malnutrition, on the other hand appetite is said to be stimulated. The cases, in which loss in weight occurs, are probably those who are at the same time addicted to some other pernicious drugs such as opium, cocaine, or alcohol. In a certain number of our cases from the well-to-do and priestly classes, an atonic condition of the voluntary muscles of the body was commonly met with. These individuals were flabby and therefore had a tendency to become obese. The appearance of bhang addicts taking excessive doses is generally sleepy and they often have a vacant look. In about 60 per cent of those indulging in Indian hemp, the conjunctivæ are congested and have a yellowish-red tinge which becomes intense when the dose is repeated.

The confirmed ganja and charas addicts, especially those taking large doses, often exhibit signs of deterioration of general health. The excessive smokers are thin, emaciated persons with a sallow or muddy complexion, and dull grey eyes. Excessive smoking also produces chronic catarrhal laryngitis and considerable bronchial irritation may result.

The daily repeated dosage of these drugs overburdens the alimentary and excretory systems, the appetite declines and food is not properly assimilated. The addicts lose weight rapidly and may suffer from general cachexia; the skin becomes pale and dry and is often covered with scales; the nails, teeth and hair, which are often affected, become dry and lose their lustre. The general bodily nutrition suffers, because the money, which should be spent for the purpose of procuring wholesome and nutritious food, is used to buy the drug itself. Impairment of vitality is thus produced, which renders the system incapable of resisting an intercurrent disease. Addicts are generally more sensitive to the vicissitudes of weather than ordinary individuals.

#### EFFECTS ON THE CENTRAL NERVOUS SYSTEM

The main effect of hemp-drug addiction is on the central nervous system. These effects can be grouped under two headings:—

A. Temporary effects, i.e., those that are only present when the person is actually under the influence of the drug.

B. Permanent effects, i.e., the sequelæ of the prolonged use of these drugs.

##### *A. Temporary effects*

Soon after taking a moderate dose by mouth the pulse increases somewhat in fullness and frequency, the face becomes flushed, and there is a feeling of warmth all over the body; the appetite becomes sharpened and there is a tendency to talk. In rare instances aphrodisiac sensations are experienced. The sensation of pain is definitely dulled and there is a feeling of partial anæsthesia all over the body. The pupils are slightly dilated.

With larger doses the above symptoms become more pronounced; the pulse becomes rapid and sometimes irregular at first and slows afterwards. The temperature varies according to whether the individual is excited or depressed. This stage is usually followed by drowsiness and deep sleep.

*Ganja and charas smoking.*—The immediate effects of moderate doses in a habitual consumer is the initial feeling of anxiety and restlessness, which is followed by a refreshing and stimulating feeling. The sense of fatigue is alleviated, pleasurable sensations are produced so that the consumer is happy, and congenial towards everybody. Restlessness is removed and there is a quietening effect on the nervous system, which induces a sense of forgetfulness of all mental worries.

The effects in many cases are attended with hallucinations of sight, hearing, and general sensibility. The senses become hyper-acute and more subtle. Disturbance of the sensations of taste and smell may also occur during the later stages. Deep sleep generally follows in the majority of cases an hour or more after indulgence.

There are individuals amongst ganja and charas smokers on whom the effect of intoxication is quite different from that ordinarily obtained. They lose all sense of proportion and become irresponsible.

*Bhang or 'siddhi' drinking or hemp eating.*—Bhang is somewhat extensively used for occasional indulgence and for religious purposes; its symptomatology therefore deserves special mention. The effects produced by this drug are more lasting than those produced by smoking ganja and charas. With moderate doses the individual feels cheerful. The appetite is sharpened. With some there is a sensation of forgetfulness and relief from worries and troubles of life, others get good sleep after the day's hard work, still others feel active and interested in life and their surroundings, after taking a dose.

Most bhang addicts, after a regular dose, become reflex and emotional; the control of the higher centres is lost and the sense of judgment is impaired to an appreciable degree. The stage of intoxication generally lasts from three to five hours and then sleep supervenes. The addict on waking next morning does not experience any marked nausea or vomiting nor are the bowels affected (constipated) as in the case of other intoxicants. Some of the addicts complain of slight dizziness and congestion of the eyes and feeling of heaviness in the head on waking next morning.

*Duration of effects. Ganja and charas smoking.*—Smoking produces its effects more rapidly than consumption by the mouth because by the latter method the absorption of the resin, which is combined with large quantities of colloidal matter, is considerably delayed from the gastro-intestinal tract. With pure resin absorption is of course much quicker. According to Russell, in the case of ganja smoking the mental effects appear within three to five minutes while in the case of charas they may appear with the first pull from the pipe ('chillum'). In the case of ganja, the effects last from half to one hour or even longer, in the case of charas from 15 to 20 minutes. With bhang the symptoms may set in from 20 to 30 minutes or may be delayed and may last from two to twelve hours.

#### B. Permanent effects

*Mental effects.*—Mental injury is more likely to occur in the case of those individuals who take large doses and for prolonged periods.

The effects of different preparations are interesting. Emotional character and judgment are affected more in the case of bhang, while memory

and sleep are more disturbed in the case of ganja and charas. Bhang habitués were also more peevish and hypochondriacal than those indulging in ganja and charas. The incidence of gross injuries to the central nervous system such as insanity and moral depravity appears to be more frequent amongst the ganja and charas habitués than the bhang drinkers. Epileptic fits are, on the other hand, more frequent amongst the bhang habitués.

*Effects on sleep.*—We are inclined to believe that sleep is disturbed more in the case of ganja and charas addicts and little or not at all in the case of those addicted to bhang. This may be due to the fact that bhang as a sedative has a mild and prolonged action, while ganja and charas have rapid and intense effects in which euphoria and stimulation are more pronounced.

*Use of the hemp drugs in relation to mental disorders and crime.*—We have come across a few instances of insanity resulting from the abuse of bhang or charas or ganja. The testimony of many of the competent medical authorities in this country also sponsors this belief. The abuse of hemp drugs injures the constitution in the same manner as an excessive indulgence in any other narcotic drug. It does not necessarily produce insanity, except perhaps in those who have predisposition to it. It may, however, lead to rough manners and apathy and extraordinary behaviour on the part of the individual. Those who smoke ganja and charas excessively are often quarrelsome and do not heed the consequences of their deeds. We have examined records of murder and crime cases in jails and mental hospitals and have found that only in a very few instances (1 to 2 per cent) the temporary or the permanent mental derangement induced by hemp drugs was directly responsible for a crime.

As regards the relationship between hemp-drug addiction and crime, there are instances where the addicts committed criminal acts under the effect of these drugs, especially after smoking ganja or charas, under grave provocation or in cold blood and with premeditation. Such instances do not necessarily prove any definite relationship between hemp drugs and crime. Indulgence in alcohol undoubtedly gives rise to a feeling of bravado and courage by depressing the higher controlling cerebral centres, and there are many instances in which it has led to crime of a very grave nature. With regard to hemp drugs, however, the situation may be viewed from a different angle. Hemp drugs are cheap and are generally used by the poorer classes, who belong to the lower strata of society, to which most of the criminals in this country belong. This may be an explanation of the fact that proportionately more consumers of hemp drugs, especially ganja and charas smokers, are found among bad characters than among the population in general. Moreover the associated poverty of the addicts may lead them to commit thefts and other petty offences, but

this does not throw the entire responsibility on the hemp drugs.

So far as premeditated crime is concerned, especially that of a violent nature, hemp drugs in some cases may not only not lead to it, but they may actually act as deterrents. The result of continued and excessive use of these drugs, in our opinion, is to make the individual timid rather than to lead him to commit a crime of violent nature. Our opinion in this respect, based on the study of a large series of addicts, is that the tendency of the drug appears to be to develop or bring into play the natural disposition of the consumer and to emphasize his true character and peculiarities.

#### TYPES OF HEMP-DRUG ADDICTS

There is nothing inherent in the make-up of a normal individual which draws him towards the habitual use of narcotic drugs. The basic factor underlying addiction is always some defect or abnormality in the mental make-up of the individual. The causes leading to drug addiction are almost identical all over the world. The reasons for which the habit is started are psychological and are sufficiently convincing to the addict himself and he intentionally carries on the habit in spite of being aware of its dire consequences. The addicts in this country can be divided into four main groups :—

Group I.—Persons belonging to poorer classes, such as day labourers, or domestic servants. These people are the principal consumers of ganja and charas. They keep to small doses and as a rule suffer from little or no injury to their general health.

Group II.—Those individuals who use these drugs in the same way as opium, for their narcotic effects. The members of this group are idlers and persons below average mental equilibrium. Ganja and charas are mostly used by this group and the damage to their health is more perceptible than in the case of group I.

Group III.—Those who use hemp drugs in order to obtain stimulant effects combined with intoxicating effects in the same way as from alcohol. This practice exists mostly amongst the idle rich.

Group IV.—Mostly religious mendicants (sadhus and fakirs) and the priestly classes. Hemp drugs are used in all forms by them in order to overcome the feeling of hunger and in order to help them to concentrate on religious and meditational objectives, and also sometimes by the unaccustomed to excite passion and emotion.

#### SUMMARY AND CONCLUSION

(1) The hemp plant grows wild over extensive tracts in northern India along the southern slopes of the Himalayas, coming well down into the plains. Its cultivation for narcotic purposes is strictly controlled and is confined to selected areas under careful supervision of the excise authorities.

(2) The resinous substance contained in the hemp plant is the active principle responsible for its physiological activity. The resin, as obtained from the plant, contains a number of compounds, one of these being *Cannabinol* which is probably the active principle. The potency of hemp drugs deteriorates with age.

(3) *Charas* and *ganja* are preparations from the same plant and differ in the amount of the narcotic principles they contain; the physiological effects produced by them are similar, differing in degree. Ganja and charas are mostly smoked, while bhang is usually taken by the mouth in the form of a beverage.

(4) The present use of hemp drugs in India may be considered under three main headings:—(i) use in connection with religious and social customs; (ii) medicinal uses; and (iii) use for narcotic and euphoric purposes.

(5) The use of hemp drugs in order to produce euphoria and mild stimulation, although still common, is gradually declining. It exists mostly at the present time among the lower and working classes.

(6) As euphorics, hemp drugs, unlike alcohol, rarely produce severe intoxication, especially in those who take them habitually. Abuse of these drugs sufficient to produce intoxication of a pronounced type exists only amongst the idle and vicious classes in the cities and towns.

(7) The total consumption of hemp drugs in British India during the year 1934-35 amounted to 1,031,496 lb., which works out approximately at 4.24 lb. per 1,000 of population per annum (according to the census figures of 1931) as compared with 15 lb. during 1912-13. The United Provinces are the largest consumers of hemp drugs, next in order come the Punjab, Bengal, Bombay, and Central Provinces and Berar, respectively.

Charas is mostly used in the northern and western parts of India, i.e., the North-West Frontier Province, the Punjab and the western districts of the United Provinces. In Sindh, Rajputana, and western districts of the Punjab and the United Provinces, bhang is more commonly used in the form of a cooling and refreshing beverage suitable for the hot and dry summer months. In the rest of India, i.e., Bengal, Bihar and Orissa, Bombay, Madras, etc., ganja is the drug of choice.

From the survey we have carried out and from the total consumption of hemp drugs and daily dosage of addicts we have roughly estimated that there are at least between 855,844 and 1,000,000 hemp-drug addicts in this country, i.e., approximately 0.3 to 0.5 per cent of the population of this vast country take hemp drugs habitually at the present time.

(8) The moderate use of ganja and charas may or may not be attended with harmful effects, while in the case of bhang there is definite evidence that no harm may result to the general health with moderate doses. On the other hand confirmed ganja and charas addicts, especially

those taking large doses, often exhibit signs of deterioration of general health. The daily repeated-doses, especially if large, overburden the digestive and the excretory systems with the result that the appetite is lost and food is not properly assimilated.

(9) Hemp drugs are, even at the present time, used as sexual stimulants by the lower classes. They lead to temporary stimulation of the psychic areas, and the mental excitement thus resulting gives the semblance of aphrodisiac effects, especially in those individuals who are sexually inclined.

The incidence of sterile marriages amongst hemp-drug addicts worked out to nearly twice that of the normal population.

(10) Effects on the central nervous system can be divided into two stages: (a) an initial stage of stimulation and exhilaration, and (b) a stage of depression when the sedative effects become more marked. The effects during each stage are largely influenced by racial and personal idiosyncrasy and may be entirely modified by the individual temperament.

(11) From a careful study of a series of 1,238 addicts we are inclined to believe that continued

and excessive indulgence in these drugs tends to impair the normal functioning of the nervous system, renders the addict incapable of mental exertion, and causes general debility and premature decay.

(12) We have come across a few instances of insanity resulting from the abuse of bhang or charas or ganja. The abuse of hemp drugs injures the constitution in the same manner as an excessive indulgence in any other narcotic drug. It does not necessarily produce insanity except perhaps in those who have predisposition to it.

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### HÆMATOLOGICAL TECHNIQUE

By L. EVERARD NAPIER, M.R.C.P. (Lond.)

and

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PART V of this series has been unavoidably postponed this month. It is hoped to resume their publication in July or August.

## Medical News

### BOMBAY MEDICAL COUNCIL

SUMMARY of the proceedings of the meeting of the Bombay Medical Council held on the 9th February, 1940.

The Council proceeded to consider the complaint by Dr. V. B. Mankad, M.B., B.S., and five other medical practitioners of Ahmedabad against Dr. Ganpatram Gokaldas Patel, M.B., B.S., D.O.M.S. (Lond.), in respect of the charges, *viz*,

(a) of directly or indirectly procuring, or sanctioning or acquiescing in the publication and free distribution among patients of a handbill or leaflet in Gujarati, the said handbill or leaflet commending or directing attention to the professional skill, services, popularity, amiable temper, the care and caution had by Dr. Patel in the treatment of eye diseases; it was alleged that the mention of Surya Bhuwan Hospital was intended to be an advertisement to solicit more practice;

(b) issuing cards or tickets containing not only the number and name of the patient thereon but also the name and address, etc., of Dr. Patel which, it was alleged, constitute an advertisement;

(c) under the cloak of a semi-charitable eye-clinic, it was alleged, he was carrying on private practice charging only one anna to every out-door patient of the Surya Bhuwan Eye Hospital.

These acts appear, it was alleged, to contravene the provision of clauses (a) and (m) of rule 1 in Section II of the Code of Medical Ethics and clause (a) of section 6 of the Warning Notice.

Mr. C. C. Parikh, Advocate from Ahmedabad, was allowed to appear for Dr. V. B. Mankad, Dr. D. E. Anklesaria, Dr. M. M. Parikh and Dr. M. D. Anklesaria, four of the complainants herein, as a special case.

Mr. G. C. O'Gorman, Bar-at-Law, and Mr. H. R. Pardiwalla, Bar-at-Law, instructed by Messrs. Majumdar and Dalal, Solicitors, appeared for Dr. G. G. Patel, the practitioner.

Upon the conclusion of the deliberations, the following resolution was put from the chair:—

'That the facts alleged against Dr. G. G. Patel, M.B., B.S., D.O.M.S. (Lond.), in the Notice of Inquiry have been proved to the satisfaction of the Council.'

The said resolution was declared lost, as a result whereof Dr. Patel was held not guilty of the charges preferred against him in the Notice of Inquiry.

The Council then proceeded to consider the question of amendment of rules 61 and 64 of the Rules of the Council relating to travelling allowance and passed a resolution approving of the amendments recommended by the executive committee in regard to the said rules.

The Council then proceeded to consider the question of recognition of the D.O.M.S. of the College of Physicians and Surgeons of Bombay as an additional registrable qualification and decided to grant recognition to the D.O.M.S. of the College for registration as an additional qualification and further resolved that the same be included in Table (G) of the Bombay Medical Register.

The Council then proceeded to consider the application of Dr. J. N. DeSylva, L.M. & S., for restoration of his name to the Bombay Medical Register and resolved that the consideration of his application be adjourned *sine die* and that he be asked to submit certified copy of the judgment in the proceedings now pending against him.

The Council then proceeded to consider a letter dated the 7th August, 1939, from the Secretary, Medical Council of India, forwarding therewith a copy of letter dated the 4th July, 1939, from the Registrar, South African Medical Council, Pretoria, and decided to accept the recommendation of the executive committee that any person whose name is erased from the Register of South Africa where he was formerly a registered medical practitioner for infamous conduct in a professional respect should not be entitled to have his name entered in the list of the Bombay Medical Register, provided the Medical Council of the said country



notifies to this Council the name of such a medical practitioner, until such time as the registering Council shall otherwise intimate and that this rule be laid down by the Council provided that the South African Medical Council is also prepared and willing to reciprocate with this Council in the like manner.

### INDIGENOUS DRUGS INQUIRY

ADVANCE in knowledge of the pharmacopœia and allied drugs produced in India and development of local drug manufacture, bringing prices within easy reach of large masses in India are some of the achievements claimed for the study, of a large number of Indian medicinal plants under the Indigenous Drugs Enquiry, financed by the Indian Research Fund Association. The study ranged over a wide field from the isolation of the active principles to tests of action on animals and, in suitable preparations, on patients.

A number of manufacturing firms have come into existence and instead of concentrated extracts which were formerly imported, practically all kinds of galenical preparations, powders, etc., are now being manufactured in India, in many cases, from material locally produced. The growth of the pharmaceutical industry has, in its turn, stimulated the manufacture of solvents such as alcohol, chloroform, ether, benzene and many coal-tar products used in medicine.

There is now greater demand for indigenous raw material and with this increase in demand, there has been an increase in the area under drug cultivation. Belladonna, digitalis, hyoseyamus, squills, colchicum gentian, artemisia, juniper, valerian, podophyllum, colocynth, ephedra, pyrethrum, etc., are a few of the drugs which have come into more extensive use. Raw products of good quality are now more easily available at reasonable prices and the export of crude drugs such as belladonna, ephedra, podophyllum, chaulmoogra, castor oil seeds, etc., has gone up considerably.

Attempts are being made to grow the plants in such a manner that the maximum quantity of active principles can be obtained, while to overcome difficulties in identification, a herbarium of medicinal plants is being got ready. Digitalis, ipecacuanha, pyrethrum are some of the important drugs, the cultivation of which is being thus encouraged. It is hoped that with proper development, India will not only be able to meet her requirements of medicinal herbs and drugs but also have a large residue for export.

The researches have done much to prove or disprove, by the application of modern methods, the therapeutic value of many drugs used in indigenous medicine. Of the drugs, the efficacy of which has been proved, Isabgul (*Plantago ovata*), Kurchi (*Holarrhena antidysenterica*), Sarpagandha (*Rauwolfia serpentina*), Babchi (*Psoralea corulifolia*), Kuth root (*Saussurea lappa*), cobra venom, are a few which may now be admitted into the Indian Addendum to the Pharmacopœia and, later, into the Indian Pharmacopœia. On the other hand, a number of drugs, which were in the old addendum, have been shown to be worthless.

As a natural corollary to work on the medicinal plants, a systematic study has been undertaken of the poisonous plants growing in India. The work is of importance not merely to the medical profession, but also to the veterinarian and to those interested in livestock. The toxic effects of plants in common use, such as aconite, barringtonia, calotropis, nerium, etc., have been worked out, and steps taken to warn people against their indiscriminate use by unqualified practitioners.

Some common food poisons, such as Khesari dal (*Lathyrus sativus*), Indian millet (*Sorghum vulgare*), Sialkanta seeds (*Argemone mexicana*), which have been responsible for serious outbreaks of poisoning in men and animals, have also been studied. Only the fringe, however, of this vast problem of poisonous plants and food poisons have so far been touched.

Investigations have also been made on the diagnosis and treatment of such diseases as malaria, amœbic dysentery, kala-azar, filariasis, diabetes, etc. In order to find out whether climatic factors and variability of

the strains of parasites make any difference in the effectiveness of drugs, indigenous drugs as well as drugs and synthetic preparations manufactured in India and abroad have been subjected to careful tests. The minimum effective doses of antimalarial and other drugs, required to bring about disinfection of the patient in a reasonably short time, are being worked out, so that treatment may be carried out with the minimum of expense.

The Indian Indigenous Drugs Enquiry was started in 1926 at the School of Tropical Medicine, Calcutta, with its well-equipped pharmacological and chemical laboratories, where the chemical composition of crude drugs could be determined and their biological action on living tissues evaluated. The clinical testing of drugs were carried out at the Carmichael Hospital for Tropical Diseases which is attached to the Tropical School as its research hospital, the only one of its kind in the East.

The main objects which the enquiry had in view, were to make India, as far as possible, self-supporting in her supply of drugs by making possible the utilization of indigenous drugs in a form suitable for administration; to discover remedies suitable for application by exponents of Western medicine from among those claimed to be of high value by Ayurvedic, Tibbi and other indigenous systems of medicine; to find means by which efficacious remedies could be brought within the reach even of the poor, and finally to prepare an Indian Pharmacopœia.

The Indigenous Drugs Enquiry brought to light the true state of affairs with regard to the quality of drugs on the market in India and, eventually, led to the appointment of the Drugs Enquiry Committee and finally to the establishment of the Biochemical Standardization Laboratory of the Government of India.

The pioneer work of the Indian Research Fund Association has also given an impetus to research on Indian medicinal plants in many places in India. Investigations have been started in the universities and colleges at centres such as Calcutta, Bombay, Dacca, Patna, Allahabad, Lahore, Madras and Trivandrum.

### MEETINGS OF THE UNITED PROVINCES MEDICAL COUNCIL HELD ON 17TH NOVEMBER, 1939, AND 18TH MARCH, 1940

THE Delhi Medical Association's resolution, dated the 11th March, 1939, regarding immigration of foreign medical practitioners into this country, was considered and the council passed the following resolution:—

'The United Provinces Medical Council strongly protests against the immigration into this province of foreign medical practitioners, not registrable anywhere in the Empire—much less in these provinces, also against the fact that no bar has so far been placed against their practising medicine and surgery.

This council unanimously recommends to the Government to take early steps in the shape of adequate legislation to (i) prevent unrestricted immigration of such practitioners for the purpose of practice into this province, and (ii) to prevent them from practising in the United Provinces since they are neither registered nor possess any registrable qualification.

In this connection, the council brings to the notice of the Government the fact that Indian Nationals are not allowed to practise in their countries of origin even if they have qualified as doctors in those very countries.

Further, this council views with great disfavour the association or covering of unregistered foreign medical practitioners by the medical practitioners registered under the United Provinces Medical Act.

In view of the influx of many men who practise medicine and surgery and about whose qualifications nothing is known, the question as to what constitutes an unqualified person was considered.

The question of restoration of the name of Dr. Kanhaiya Lal, L.M.P. (Reg. no. 2957) was considered and it was resolved that his name be restored free of charge and without any affidavit.



The question of restoration of the name of Dr. Ram Saran Das Bejal, L.M.R. (Reg. no. 729) was considered and it was resolved that his name be restored provided he submitted an affidavit to the effect that he was the person who was originally registered under certificate no. 729, but no affidavit to the effect that to his knowledge no proceedings for removal of his name were ever taken against him be obtained. It was further resolved that this practice be followed in similar cases in future.

Resolved that the name of Dr. Ram Saran Das Bejal (Reg. no. 729) be restored to the medical register, free of charge and without obtaining any declaration, as the case is known to Captain Bagchi. Resolved further that no rules on the point are necessary but in future each such case be referred to the council to be judged on its merits, while the Bengal procedure be followed in the restoration of names removed for want of address. Rest of the minutes be confirmed.

Resolved that the name of Dr. Ivy Keess, W.M.S. (Reg. no. 1963), be restored without obtaining a declaration and free of charge, as she is known to Dr. Caul.

The action of the President in requesting Government to prosecute, under the Indian Medical Degrees Act, (i) Midwife Mrs. Bala Saxena (*née* S. Dass) and (ii) Mr. S. S. Singhal, Director, The Indian Medical Society, Aligarh, was confirmed, and it was resolved that that it may be pointed out to Government that this council has no powers to deal with the case of Mr. Singhal in the manner suggested and that Government should be requested to take further action in the matter.

Resolved that the State Medical Faculty be informed that this council is prepared to restore the name of Mr. Mahmud Ali (late Reg. no. 840) to its medical register if the State Medical Faculty restore his diploma. Mr. Mahmud Ali may then be asked to comply with the formalities.

The report of the Standing Committee, which met on 28th February, 1940, was considered to approve their recommendations.

*Recommendation no. 1* was accepted subject to the following changes and it was decided that the Bombay Medical Council be informed:

(i) *Delete* the following paragraph from the footnote proposed to be added to item 1(c) of the Code of Medical Ethics, *viz*:

'The United Provinces Medical Council takes a similar view of the association of a medical practitioner with any system or method of treatment which is not under medical control and which is advertised in the public press.'

(ii) The last paragraph of the proposed footnote should read as follows:—

'In the above findings the United Provinces Medical Council does not pretend to interfere with the right of a medical practitioner to be associated (save as above) with any legitimate business enterprise but if such enterprise concerns the sale of a medicine or food the practitioner should not allow his name, professional status or qualifications to be used for advertising purposes outside the medical press.'

Resolved that this council recommends to the Government and the Agra University that while constituting the Agra Medical College they should consider the desirability of affording opportunities to the Licentiates for obtaining the M.B., B.S. degree. This council should be given an opportunity to submit its proposals on this point before their arriving at a final decision.

## ST. JOHN AMBULANCE AND RED CROSS

THE ANNUAL GENERAL MEETING OF THE ST. JOHN AMBULANCE ASSOCIATION AND INDIAN RED CROSS SOCIETY, HELD ON 26TH MARCH AT THE VICEROY'S HOUSE

THE Viceroy said 'India has not escaped the infection of the discords and rivalries which have disfigured the world's history and retarded its progress of late.

Amidst all these, and in contrast to them, it is heartening to see two Societies, both of which had their beginnings in the strong desire to relieve the toll of suffering caused by war, going steadfastly forward, hand in hand without competition, confusion or discouragement, jointly dedicated to the service of humanity, which so sorely stands in need of it to-day.

The work which your Societies have done in peace is admirable, but, inevitably, it is in time of war that the test and the strain is heaviest. It was therefore with particular attention that I read the reports and listened to the interesting summaries which have just been presented to us by Sir Ernest Burdon and by General Jolly of the work that has been accomplished during a year in which we have been living partly under the shadow of imminent war and partly in a state of war itself.

There is every cause for satisfaction with the work that these reports reveal, and especially the report of the Central Joint War Committee. It was no small task to bring the Mobilization Plan so smoothly into operation, and those responsible for it, both at Headquarters and on the Provincial Committees, fully deserve the compliments which have been paid to them in the speeches we have heard. I am happy to feel that the work so well prepared and begun is continuing with the smooth efficiency we should expect under the able guidance of the Red Cross Commissioner.

The work of the Joint War Committee involves a close co-operation with Army Headquarters, and it was in that sphere that the willing help and counsel of General Tabuteau, whose loss we mourn to-day, made itself particularly felt. I will not add to the tributes you have already heard paid to him, except to say that no one more richly deserved the honour recently conferred upon him of admission to the rank of Commander of the Order of St. John.

It is a matter of regret to all of us that this is the last Annual General Meeting which Sir Ernest Burdon will be attending. Three years ago, the first of these meetings over which I presided, was also the first at which Sir Ernest was present as Chairman of the St. John Ambulance Association and as a Knight of Grace. His energy, his balanced judgment and his ripe experience have combined to make him the ideal Chairman and Chief Commissioner. We shall miss him very much.

Mr. Badenoch, whom I have nominated to succeed him as Chairman, needs no introduction either to you or to the work and responsibilities which await him. As Honorary Treasurer of both organizations he has already to his credit much valuable work, and I am sure that he will prove an able successor to Sir Ernest Burdon.

I feel sure, too, that you would wish me to welcome to-day, on your behalf, General Jolly, to this his first General Meeting as Chairman of the Indian Red Cross Society.

Dealing, first, with the St. John Ambulance Association and Brigade, I was delighted to hear that 1939 had been a record year of achievement, both in the field of instruction in First Aid and Home Nursing, and in increase of membership of the Brigade. Eight thousand members does not sound a large number in this country of hundreds of millions, but it represents a leap forward in membership by 60 per cent in one year. For this the war is no doubt responsible, but war or no war, let us hope that this increase will have set the standard for the years to come, for India has and will always have need of as many trained workers, as she can get, of the type that are found in the St. John Ambulance Brigade. It is a matter of great satisfaction that the organization of the Brigade on a territorial basis coinciding with Provinces, under the control of heads of Civil Medical Departments, has been completed. This arrangement, I am sure, will greatly assist to maintain the efficiency of the Brigade in India.

We may hope that there will be no call in India to put into practice A. R. P. and anti-gas training provided by St. John Ambulance, but the importance of having

ready a supply of volunteers skilled in such measures needs no emphasis from me.

The Mobilization Plan and the formation of the Joint War Committee made it inevitable and proper that the Red Cross and St. John Ambulance should share the burden of and the credit for much that has been accomplished during the past year. In particular I would like to mention the Women's Auxiliary Corps in Bombay the numerous work parties that have been formed up and down the country, typical of which is the party that works so zealously here in Delhi under the guidance of Lady Cassels, and the organization of a Voluntary Aid Service of Nurses to supplement the Nursing Branch of the Army Medical Services. These are all solid achievements of great value, within the scope of both organizations.

Let me mention now some matters which pertain more particularly to the Indian Red Cross Society. I was most interested to hear of a Blood Transfusion Service in Bengal. This is an example which I hope will spread.

I hope, too, that the donation from the British National Institute for the Blind, which has been spent upon education work on the prevention of blindness, is a seed that will multiply a hundredfold. My appeal for funds for St. Dunstan's Hostel, and Sir Clutha Mackenzie's recent tour of India (though St. Dunstan's, of course, works only for the war blinded) have, I think, roused interest in the grave problem of blindness in this country and have perhaps inspired the hope that much might be done here by way of prevention, cure and after-care, in co-operation with the great institutions which already exist outside India for the purpose.

It is gratifying to note that the Society in India has been able to extend help to other parts of the world, which stood in need of it, and that two nurses in India have been awarded by the International Red Cross Committee the distinction of the Florence Nightingale Medal. This, and the fact that the war has not yet curtailed the normal peace-time activities of the Red Cross in India, betokens good organization and reserves of strength. But there is no doubt that those reserves still need most urgently to be built up both in members and in funds, against a severer testing time which may yet be in store. The response by the public to my appeal for funds for the Red Cross and St. John Ambulance—which was greatly assisted by the willing co-operation of the Press—has been generous, especially considering the claims of other War Funds. But there can never be too much generosity in such a cause, and I feel sure that if and when the greater need arises it will be found that the springs of public support in India have barely yet been tapped.

War is an evil thing, but out of war have arisen such symbols as the Red Cross of Geneva and the eight-pointed White Cross of St. John of Jerusalem, the arms of which represent the virtues of prudence, temperance, justice and fortitude. These are ancient symbols, and they have undoubtedly helped to lead the world along the paths of humanity and progress. The shadow of another symbol, not so humane, is now brooding over our civilization. When it has passed, mankind will still need the services of those who work under the Red Cross and the Cross of St. John; they will not be found wanting, and they will come to their work, I know, with strength renewed and with their chivalry untarnished.

## Current Topics

### The Use of Colloidal Aluminium Hydroxide in the Treatment of Peptic Ulcer

By JOHN F. McINTOSH

and

COLIN G. SUTHERLAND

(Abstracted from the *Canadian Medical Association Journal*, Vol. XLII, February 1940, p. 140)

In recent years there has been a tendency to avoid the use of absorbable alkalis in the treatment of peptic ulcer, and to search for antacid substances which do not affect the acidbase equilibrium of the body as a whole. Among these newer substances may be mentioned mucin, magnesium trisilicate and colloidal suspensions of aluminium hydroxide.

The use of aluminium hydroxide in the treatment of peptic ulcer was introduced in 1922 by Roch, who reported favourably on its clinical use. Since this time a considerable number of clinical articles have been published. All of these have been favourable, and all attest to its value in relief of symptoms. Careful studies of its mode of action have also been made. The direct effect of the drug in controlling the acidity of the stomach has been studied by several authors. A recent paper by Bennett and Gill presents clear-cut evidence that the free hydrochloric acid of the gastric secretion can be completely and continuously neutralized by its use. It is well established that aluminium is not absorbed from the alimentary tract. It has been shown that its use does not lead to alkalosis or other disturbance of the acid-base balance of the body. By inference one would expect that its ingestion would not be followed by 'rebound' acidity or hypersecretion of acid, and it is generally agreed that such is the case. Indeed, Babkin found an inhibition of gastric secretion in dogs as an after-effect, rather than an increase. Similarly Einsel has presented evidence that prolonged ingestion of aluminium

hydroxide cream by ulcer patients leads to a marked diminution in titratable gastric acidity after alcohol stimulation in comparison with acidity curves determined before treatment was begun. Woldman and Rowland have introduced a method of administration through a nasal catheter which has considerably increased its effectiveness in intractable cases and in hæmorrhage.

The present report is based upon the clinical use of an aluminium hydroxide preparation in 38 cases of peptic ulcer, some of them from the Out-patient Services, the others from the medical wards. The group comprises all the cases which came under observation during a certain period, and in which the drug was used in adequate dosage for at least a week. Cases in which the diagnosis of peptic ulcer was in reasonable doubt have been excluded, as have cases in which ulcer was established but in which there was reason for attributing the symptoms to some associated condition, such as permanent pyloric obstruction or gall-bladder disease. A synopsis of the groups of cases and results of treatment is given in table I.

TABLE I

Group		Success-ful	Unsuccess-ful	Total
1	Out-patients ..	7	0	7
2	Ward cases, uncomplicated.	18	1	19
3	Cases with gross hæmorrhage.	9	1	10
4	Cases complicated by infection.	0	2	2
	TOTALS ..	34	4	38

**Group 1. Out-patients.**—This group of cases, seven in number, comprises six cases of duodenal ulcer without complications, and one of jejunal ulcer, all proved by x-ray examination and showing evidence of active ulceration. The patients were allowed to follow their usual occupations throughout the course of treatment. In some cases frequent feedings were advised, with milk freely used as an 'interval' feeding; as improvement occurred, three regular meals were instituted, with restrictions. Aluminium hydroxide was prescribed, usually as two drachm doses, at first six times a day, later two or three times a day, as improvement occurred. All of these did well.

Several points of interest arise from the consideration of this small group of ambulatory cases. The patients took the preparation readily, and, even when due allowance is made for the possible effects of suggestion, seemed to experience marked symptomatic benefit. Five of the seven cases were re-examined after treatment had been continued for several months, and in none of these did an ulcer crater persist. In one case, in which an exploratory operation was carried out some time later, there was operative proof of cure. Only one complaint arose from the use of aluminium hydroxide. Several complained that it caused constipation. This was not sufficient to interfere with continuation of treatment, and was easily controlled by mineral oil. The literature makes frequent mention of this effect of the drug.

**Group 2. Ward cases, uncomplicated.**—This group of 19 comprises 15 cases of duodenal and 4 of gastric ulcer. Five were recent but the majority were of long standing. The average duration of the 14 chronic cases was ten years. Cases with intestinal obstruction or permanent pyloric obstruction have been eliminated, although six which showed some degree of gastric delay have been included. These cases on the average are more severe and intractable than the ambulatory cases in group 1. Hospital stay varied from one to ten weeks though two to three weeks was the usual duration, not long enough to reach an opinion as to the final outcome of treatment. Some have been followed as out-patients and others by questionnaire, so that further information is available in ten cases.

The diet and dosage of aluminium hydroxide used in this group will be discussed below, along with the other groups of hospital cases. As to the immediate effect of treatment this was very satisfactory. Pain was relieved usually in the first two or three days, and usually without the use of atropine or other drugs. It is difficult to apportion the benefit from bed rest, diet, and medication in judging this group of cases, except as a matter of personal judgment. With this qualification we may say that the immediate effect of the drug was very satisfactory indeed and compared favourably with any other form of medical treatment. On discharge all the patients were considered improved.

In eight of the ten cases in which follow-up information is available, progress has been satisfactory, although only one patient has been able to give up treatment altogether. One, under observation in the out-patient department, has suffered a recurrence of symptoms. She has stopped taking aluminium hydroxide on account of constipation, preferring an antacid which has a laxative effect. The tenth case must be regarded as a failure of medical treatment although the immediate effect was considered to be good.

**Group 3. Cases with gross hæmorrhage.**—This group comprises nine cases of duodenal and one of gastric ulcer. One patient had no symptoms before the hæmorrhage which caused his admission. Like the previous group, the average duration of the chronic cases was ten years, and the usual hospital stay two or three weeks. Two of the cases were given Meulengracht's diet, the others 'bland', or Sippy diets. Aluminium hydroxide was given by mouth usually every two hours, in one or two drachm doses. With one exception all the patients in this group did well.

Hæmorrhage ceased, pain when present was relieved, and all were able to leave hospital improved.

This series of ten cases is too small to reach a final conclusion as to the value of aluminium hydroxide given orally in the treatment of gastric and duodenal hæmorrhage. Woldman has reviewed the mortality rates reported in eight recent series of cases of hæmorrhage, and in these the fatalities have ranged from 10.7 to 22.6 per cent. In his own control series of 38 cases there were 11 deaths—a mortality of 28.9 per cent. Hence among our cases one to three deaths might have been expected, although none occurred.

Until recently medical treatment of hæmorrhage in peptic ulcer comprised starvation—withholding all solids and giving only ice-water by mouth, in order to avoid dislodging the clot by food or peristalsis. Meulengracht deserves great credit for breaking with this tradition, and allowing liberal meals to his cases of hæmorrhage; by so doing he reduced the mortality rate in his wards from 7.9 to 1.5 per cent. Alvarez and Carlson suggest that the food neutralizes the acid of the gastric juice, and so protects the clot in the aperture of the bleeding vessel from digestion. Woldman points out that the optimum acidity for peptic digestion is between pH 2 and 3; about pH 5 the power of pepsin to digest protein disappears; and that blood clot placed in a test-tube with fresh gastric juice is protected from digestion by colloidal aluminium hydroxide, even at body temperature. This is the basis for the 'drip method' which he introduced, which aims at complete and continuous neutralization of gastric acidity. In 21 cases of gross hæmorrhage treated in this manner he was able to report complete recovery in every instance. Comparing his results with those of our series, it would appear that Woldman's method is to be preferred to oral administration in cases of peptic ulcer which present this complication.

**Group 4. Cases complicated by infection.**—The two cases in this group were very much alike. Both were in males in the fourth decade suffering from duodenal ulcer; one was complicated by chronic otitis media, the other by chronic pansinusitis. Aluminium hydroxide treatment over a period of months was unsuccessful in both instances. The experience with these two cases is in sharp contrast with the outcome in the preceding groups. It is well known that manifest infection of this type is a serious obstacle to healing, and calls for vigorous attention. In retrospect it seems that it was a mistake to attempt ambulatory treatment in these two cases, and that bed rest should have been advised, along with aluminium hydroxide administered by Woldman's 'drip method'.

#### DISCUSSION

The dosage of aluminium hydroxide used in these cases was either one or two drachms. Statistical examination shows that there is no advantage in the larger dose. It is difficult to generalize about the frequency of dosage. Thrice daily seems often enough to control symptoms and promote healing in some cases. In others it seems wise to begin with six doses a day, or even a dose every two hours. On the other hand there is an advantage in cutting down dosage as soon as the symptoms are under control, in order to avoid any tendency to constipation.

The difference in the properties of aluminium hydroxide and the readily soluble alkalies makes it important to consider the time of administration. The latter are commonly given about an hour after the meal, in order to control the peak of acidity. Aluminium hydroxide reacts rather slowly with acids, and much of its efficacy is lost if given an hour after food. Some of the patients discovered this fact for themselves, and preferred to take it immediately after eating. It is probably still better to give it half an hour before the meal, as advised by Kreis. Ivy has called attention to the fact that the aluminium combines with the gastric mucus to form a flaky precipitate, which adheres to the mucosa of the stomach and duodenum. A film of this nature would serve as a physical protection to the mucosa and exert an antacid action as well. Hence it seems logical that

the drug would have its best effect when given on an empty stomach.

No definite conclusion can be drawn from these cases as to the type of diet best given in conjunction with aluminium hydroxide, as failures were equally distributed between diets of the Sippy type, and the hospital 'bland' diet. It is fair to raise the question whether there is any need for diets of the Sippy type and the undernutrition incidental to their use, when the gastric secretion is modified by the presence of aluminium hydroxide.

From studies of the chemical composition of the blood it is clear that there is no tendency to alkalosis or nitrogen retention, such as sometimes follows the use of soluble alkalis. If alkalosis is already present the carbon dioxide combining power tends to fall towards normal. Bennett and Gill have been able to put this preparation to a more rigorous test than it received in our cases. They were able to give two ounces daily to a patient with renal failure, without increase in the alkali reserve.

In this series of cases the symptomatic effect of aluminium hydroxide has been highly satisfactory, and bears out the claims made for it in the literature. Its curative effect is probably measured fairly well by its value in relieving symptoms. If this is true it is fair to ask why so many patients state that they cannot give up its use, when they claim to be symptom-free. It is probable that fear accounts for the desire to continue its use. For this fear, of course, there is good basis, and occasional doses after dietary indiscretions or warning symptoms are probably of value in preventing relapse.

In this series there have been four definite failures in 38 cases (10.5 per cent). Einsel reported nine failures in 110 cases (8.1 per cent), while Jones reported one failure in a group of 24 cases (4 per cent). In the cases recorded as failures, symptomatic relief was usually not satisfactory from the first. It is possible that some of these would have responded better to Woldman's method. It seems reasonable to consider that cases which have severe symptoms and long histories, and cases with radiographic or other evidence of penetrating ulcers should be treated in this manner, as well as cases with severe hæmorrhage.

#### CONCLUSIONS

It seems justified to conclude that aluminium hydroxide offers many advantages over the older remedies in the treatment of peptic ulcer and that its properties are such as to call for reconsideration of the principles involved. Hitherto, conventional treatment has been based upon a regimen of small meals, frequent feedings, the use of absorbable alkalis to control acidity and of atropine to control secretion. Each of these measures has its disadvantage. There is good evidence that frequent feedings are an undesirable stimulus to gastric secretion, and that absorbable alkalis lead to 'rebound' acidity. It is fair to say that treatment by conventional methods has been a disagreeable ordeal, frequently made worse by hunger, deficiency states, and the symptoms of atropine poisoning.

It is evident that aluminium hydroxide has proved itself to be a highly effective antacid without danger of 'rebound' activity. Although it may be used in conjunction with frequent feedings, these are no longer required to control acidity, and one may safely dispense with them if sufficient hydroxide is given. There is evidence that the drug has a tendency to inhibit gastric secretion when given over a considerable time. Finally its use is compatible with the present-day tendency to give more generous meals during treatment.

#### Treatment of Infected Burns

By B. C. MURLESS, M.B., B.Ch., F.R.C.S. (Edin.),  
M.R.C.O.G.

(From the *Brit. Med. Journ.*, Vol. I, 13th January, 1940, p. 51)

THE literature on the treatment of burns is legion. A great number of publications followed the introduction

of the use of tannic acid by E. C. Davidson of the Henry Ford Hospital, Detroit, in 1925, which has revolutionized this branch of surgery. Many writers since have published modifications of the original technique described, with reports showing excellent results. It is therefore with some trepidation that I venture to add to a subject so extensively investigated. The tremendous increase of burns in war-time surgery may, however, render this short article of interest now, and the somewhat rare opportunity of treating and watching the progress of eighteen cases of severe burns from one of His Majesty's ships seems worth recording.

#### THE USE OF TANNIC ACID

The functions of tannic acid are twofold. First, in the early stages it prevents the absorption of toxins by combining with proteins and their metabolites to form a coagulum; and, secondly, the coagulum formed exercises a protective action. Suffering and shock are prevented by the protection of exposed nerve endings, but equally important is the effect of the coagulum in rendering the surface free from outside disturbance and guiding the growth of the new epithelium.

For practical purposes a burn may be considered like any flesh wound, healing proceeding most rapidly in the absence of bacterial infection. Such conditions are of course ideal for tannic acid treatment, the burnt area being rendered aseptic by cleaning before the tannic acid is applied. In war time the difficulties of thoroughly cleansing burns are many, and delay must often occur. Severe shock may contra-indicate anaesthesia or any active treatment; transport difficulties are bound to delay the arrival of cases at the theatre. Consequently, though they may have received preliminary treatment, many burns met with under war-time conditions must be of the septic variety, and it is with such cases that this article is concerned.

#### TANNIC ACID IN SEPTIC CASES

Burns which have been left for forty-eight hours or more may be considered septic, as no amount of treatment with ether or spirit will render them surgically clean. Difference of opinion exists as to the use of tannic acid in septic cases. Some surgeons prefer picric acid dressings unless the burn has been cleaned within forty-eight hours. Hamilton Bailey states that tannic acid treatment may be instituted as late as seventy-two hours. The cases reviewed here may help to support the contention that there is no time limit after which tannic acid treatment should be abandoned, and that good results may be obtained by its use where sepsis is fully established.

When applied to a septic surface tannic acid will form a coagulum more readily than on a surgically clean area. A crust soon dries which, if it stays in place and can be kept hard, will supply the rest and protection essential for the healing of the inflamed tissues beneath. Such treatment may be compared with that adopted by Winnett Orr for open fractures and by Dr. J. Trueta for infected wounds in Spain. The essential advantages of this method are that the surface remains undisturbed, the covering allowing epithelium to grow in from the edges, at the same time preventing the formation of fibrous tissue and piled-up granulations, which are nearly always seen when infected burns have been treated by constantly changed dressings. The speed of epithelization with such treatment is infinitely greater than when the surface is disturbed daily, and the saving of pain and discomfort to the patient beyond estimation.

#### PUS FORMATION

Pus will usually collect beneath the crust and may form in patches, or almost the whole crust may be slightly raised and fluctuation may be present. The usual teaching of removal of or incision into the coagulum under such circumstances was not adopted in these cases. If an expectant attitude is taken, within twelve hours the pus will always find its way out at some point. It may come through cracks in the coagulum, especially at joint flexures, or may ooze out



at the edges. After discharging for a short time suppuration will cease, and any part of the crust which has become softened may be resprayed with tannic acid and dried. Not unnaturally the smell during the suppurative phase is somewhat unpleasant, but it is not nearly so bad as that encountered in the closed treatment of infected fractures.

#### FEVER AND PAIN

Nearly all cases register a rise in temperature during this treatment. It may reach as high as 104°, but this should not cause undue anxiety, and should not be considered an indication for removal of the coagulum. In most cases the fever subsides in from two to three days.

The absence of pain during tannic acid treatment is well known to be remarkable, and the same fact applies when it is used for septic burns. Following the first application and drying little pain is experienced. A feeling of tenseness and heat sometimes exists for a few hours during the suppurative phase, before the pus has found its way through the coagulum, but this is soon relieved. The agonizing pain, for which anaesthesia may be necessary, when infected burns are treated by daily dressings is thus avoided, and the general condition of the patient will benefit accordingly.

#### USE OF ANTISEPTICS

When sepsis is established the use of antiseptics in combination with the tannic acid therapy cannot render the area aseptic. Any strong antiseptic is in fact contra-indicated, as it may produce further tissue damage and prevent healing. Weak solutions of dye substances may, however, be used with the object of preventing undue bacterial growth. For these cases the tannic acid was made up in flavine solution and used in conjunction with a weak solution of methylene-blue and brilliant-green. Healing was very rapid, and it is possible that these dyes also help by stimulating epithelial growth.

The danger of softening the coagulum by using a watery solution and setting free toxins, which is very real in some early cases, is not great where sepsis is present at the beginning of treatment. If, however, the electric drier is used after each application of the dye solution softening need not be anticipated.

#### DESCRIPTION OF CASES

Eighteen cases of severe burns from cordite explosions were treated in this series. All these patients were healthy men of ages varying between 18 and 40 years. In nearly all cases the hands and face were burnt. In order of severity the sites involved were: (1) dorsal surfaces of hands and forearm, (2) feet and legs, (3) face, (4) back and neck.

The degree of the burns is difficult to tabulate, as it varied in different cases and at different sites, but it may be stated that most of the men had a considerable area of second-degree burning. A fact that may be of some significance is that all had been immersed in a mixture of salt water and oil for periods varying from a half to one and a half hours. These cases were received in hospital 120 hours later after preliminary treatment in one of H.M. hospital ships. This treatment consisted of tannic acid and flavine dressings without previous cleansing under anaesthesia, which procedure was no doubt contra-indicated by the condition of the men at that time.

On admission the general condition of the patients was fair, considering what they had been through, and the danger of primary shock and toxæmia had passed. Many of them, however, were in a shocked state owing to pain and lack of sleep, and at first frequent injections of morphine had to be given. When the dressings were removed the burnt areas almost without exception were found to be septic, patches of tannic crust and solidified discharge coming off with the gauze and leaving a raw infected surface which was extremely tender. The burnt limbs were now laid on sterile towels and swabbed over with a solution of 5 per cent methylene-blue and 1 per cent brilliant-green. They

were next sprayed with a 20 per cent solution of tannic acid in 1 in 1,000 acriflavine, and the area dried with an electric hair-drier. No dressings of any sort were used. The tannic acid spraying and drying process was repeated three-hourly by day for the next forty-eight hours and the area occasionally dabbed with the dye mixture.

The crust which formed was sticky at first but soon became hard with the constant use of the drier. Great care was necessary at night to keep the burnt surface free from contact with bedclothes and towels, to which it would stick with consequent removal of the crust. The backs of the legs, the front of the wrists, the neck, and the back were troublesome in this respect, and these surfaces usually took longer than the average time to heal. The use of bed cradles and the slinging of limbs with bandages were found very helpful in avoiding this contact. A thick hard crust coloured blue by the dye was successfully formed on most surfaces. In the majority of cases pus collected below the covering and dripped from its edges or from cracks at the flexures. In no case was the crust incised to evacuate pus, but further applications of tannic acid were occasionally employed to harden patches where it had become softened.

Fever was present in all cases, the swinging temperature sometimes reaching a high level at first but always settling in a few days. Most of the severest burns were on the dorsal surface of the hand and fingers. Daily movement of the fingers was found sufficient to prevent them adhering to each other, as the usual practice of separating them with gauze was not adopted.

#### HEALING

From periods of five days onwards the crust begins to peel or break off at the edges. As soon as sufficient crust had come off, active and passive flexion of the finger-joints was started. Special attention should be given to the metacarpo-phalangeal joint, over which the new epithelium is always rather tight.

The edge of the crust as it receded was treated with the dye mixture till only a small central area was left. The patients seemed sorely tempted to pick off the edges of the crust as healing took place, a procedure which sometimes resulted in reinfection and delay in the date of their discharge. The time of healing in infected cases is considerably reduced by this method of treatment. Evidence of pus and raised temperatures disappeared in an average of three days. In most cases only a small scab of crust remained in the centre of the burn after twenty-one days, and the patients were ready for discharge. When the surface is constantly disturbed by the application of dressings the healing time is greatly prolonged. This point is well demonstrated in one case in which in the early stages of treatment additional dressings of flavine were used on the back of one hand. The crust was disturbed by removal of the gauze, and finally a Thiersch graft was necessitated by excessive granulations and delayed epithelization. Healing of this hand was not complete in five weeks from the beginning of treatment. It seems certain this would not have occurred had the surface been left to heal under the crust, as the other hand, which was just as badly burnt and which was not dressed with gauze, was fully healed, with almost full movements, in twenty-three days.

After the crust is off, the new skin, which is delicate and sometimes rather tender, is treated with sterile petroleum jelly daily. Passive stretching of the skin by flexion of the fingers was persisted with by the patients themselves until full movement was obtained. No form of splinting was used in any of these cases.

#### RESULTS

Of the eighteen patients treated one died of bronchopneumonia. It seems surprising that others did not develop chest complications, in view of the period spent in the sea. With the exception of one case, mentioned above, in which a skin graft was necessary, the remaining sixteen cases were ready for discharge within twenty-one days.

All these men were severely burnt and the burnt areas were septic on admission. Full movements at all joints were present on discharge and there were no contractures. Absence of scarring of face and hands was remarkable, and almost the only evidence of their burns was the appearance of the finger-nails.

#### CONCLUSIONS

The treatment by tannic acid and dye therapy of eighteen cases of severe septic burns has been described.

Tannic acid treatment has not failed when sepsis is established. Pus formation is not an indication for removal of the coagulum, and incisions into it are seldom, if ever, necessary.

The speed of healing is greatly impeded if the coagulum softens and comes off and gauze dressings have to be used.

Satisfactory final results were obtained. Absence of scarring and contractures was noteworthy. In burns affecting the hands normal movements and function were obtained in sixteen out of eighteen cases.

### The Prescription of Aspirin

(From the *Lancet*, Vol. I, 10th February, 1940, p. 278)

It is not uncommon for practitioners to prescribe aspirin in a suspension of mucilage and tincture of orange in preference to the more general tablet form. There has always been some little doubt whether patients should leave the bottle on the shelf indefinitely and expect the same results as are obtained from

the freshly-dispensed mixture. Tomski and Waller (*Pharmaceut. J.*, Jan. 27, 1910, p. 53) show that these doubts are not without foundation. They find that if acetylsalicylic acid (3 per cent) is dissolved in 50 per cent alcohol and kept under ordinary laboratory conditions it decomposes at the rate of about 1.5 per cent in a day, 6.0 to 6.5 per cent in a week and 13.5 to 14.5 per cent in a month, liberating salicylic acid which is a gastric irritant. They also find that a suspension of the same strength kept under the same conditions loses 0.3 per cent in a day, 1.6 to 2.0 per cent in a week and 7.0 to 8.0 per cent in a month. Their conclusion is that suspensions should be prescribed in preference to solutions in alcohol. The following prescription is a useful one:—

R. Acid. acetylsalicyl.	..	..	gr. 80
Pulv. trag. co.	..	..	gr. 40
Syr. limonis	..	..	ʒi
Aq. chlorof. ad	..	..	ʒviii
Sig. ʒfs S.O.S.			

This mixture will keep fairly well, but should be made up freshly if it is to give its maximum effect and be as little irritating as possible. Syrup of lemon is suggested because of the temporary scarcity of orange peel for the manufacture of orange preparations which, by the way, the Minister of Supply has included under 'non-essential medicines'. On the question of solutions of aspirin prepared with ammonium acetate or potassium citrate Tomski and Waller point out that the loss due to decomposition has long been established; thus the Natural Formulary recipe for 'mist. acid. acetylsal' is not to be commended.

## Reviews

**A TEXTBOOK OF X-RAY DIAGNOSIS.**—By British authors. (In three volumes.) Edited by S. C. Shanks, M.D., M.R.C.P., F.F.R., P. Kerley, M.D., M.R.C.P., F.F.R., D.M.R.E., and E. W. Twining, M.R.C.S., M.R.C.P., F.F.R., D.M.R.E. Volume III. 1939. H. K. Lewis and Company, Limited, London. Pp. xiv plus 800, with 710 illustrations. Price, £3 3s.

THE circumstance which has led to the appearance of the third editor's name on the dedication page is a sad blow to British radiology, for at the time of his death Edward Wing Twining was in the prime of life and one had a right to expect many more years of useful service from him. He however played an important part in the preparation of this volume which was in its final stages at the time of his death.

This third volume, which is by far the largest of the three, is devoted almost entirely to bones, for, though the first two hundred pages are headed 'the central nervous system', the bony supports of the brain and spinal cord loom so large in the pathology of these structures that the generalization is still more or less true. Additional methods of investigating brain tumours and other pathological processes, such as ventriculography and encephalography, alone or combined with angiography have passed out of the stage of being dangerous procedures only conducted by one or two specialists to become the routine examinations in certain conditions: this whole section is very ably written by Hugh Cairns and M. H. Tupe.

The next part is on the accessory nasal sinuses and mastoid processes. This is a branch in which considerable advances have been made in recent years, aided largely by the great precision of the apparatus available.

Part III is on bones, joints and soft tissues and occupies about two-thirds of the book and there are no less than twelve contributors including the two editors. This part is of course divided into a number of sections; of these the first is a very useful one on

normal structures, which we recommend the practitioner to study very carefully so that he is not misled by the inexperienced radiologist who has a flair for mis-interpretation and who so frequently fails to take a skiagram of the good limb for comparison. The last section, on localizations of foreign bodies, is one that is likely to be referred to very frequently during the next year or so. It is a subject in which considerable advances have been made since the last war.

The last three parts are all short ones, on the teeth and jaws, on the eye, and on cineradiography.

The third volume completes this very important work. It is a book that is not written primarily for the radiologist, though one hopes that every radiologist in the country possesses one, but for the physician and the surgeon. We cannot emphasize too strongly the importance of the physician and surgeon reading his own skiagrams and making his own interpretations, in which one hopes he will be guided by the radiologist. Physical examination has its limitations and these are fully recognized: radiography also has its limitations, but there are many radiologists who are loth to recognize this fact. The physician and surgeon can only hope to avoid becoming radiologist-ridden by learning to interpret their own skiagrams, and we know of no work that will help them to do this better than the three volumes of this excellent textbook.

**HUMAN HELMINTHOLOGY: A MANUAL FOR PHYSICIANS, SANITARIANS AND MEDICAL ZOOLOGISTS.**—By Ernest Carroll Faust, A.B., M.A., Ph.D. Second Edition. 1939. Henry Kimpton, London. Pp. 780. Illustrated with 302 engravings. Price, 40s.

NINE YEARS have elapsed between the appearance of the first and second editions of this book, and during this interval there have been many advances in our knowledge of helminthology as applied to human beings, and most of these have been incorporated in the new edition. This applies, among other conditions,



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especially to strongyloides infection and creeping eruption.

For the most part the figures are the same but about twenty have been added, fifteen altered or modified, and six or seven omitted. Advantage, in substituting newer and more accurate figures, has not always been taken, however.

In nomenclature we are pleased to note that the list headed 'Names of parasitic helminths of man and pathological designations for infections with these parasites' has been to some extent modified and every infection is not now invariably named after the generic name of the worm with the affix 'iasis' followed by the specific name. But we note that this modification has not been carried as far as we consider it might have been, for instance in the first edition 'Heterophyiasis heterophyes' and 'Heterophyiasis katuradi' both appeared and they are replaced in the new edition by 'Heterophyes infection' for both of them, this is all to the good, but then we note 'Hymenolepiasis diminuta' and 'Hymenolepiasis nana' still appear in the new edition. Such inconsistencies can be indefinitely multiplied if the two lists are compared closely. We regret that the author, having withdrawn some of the absurd names he concocted for his first edition, did not complete the purge and slaughter them all in the second edition.

There are a few spot maps showing the world distribution of certain important worm infections. Such maps, unless they are accurate, are better omitted, otherwise they will lead astray the inexperienced, with perhaps serious results. A glaring example is that in the distribution of *Echinococcus granulosus*, India is shown as free from this infection. The map was wrong in the first edition and has been reproduced in the second.

We are glad to see that the names *Fulleborniidae* and *Fullebornius* have been dropped and the old names *Dracunculidae* and *Dracunculus* re-established.

There is a new chapter on anthelmintics in general with a fairly detailed description of all the important drugs in this class. This, like all summaries, contains many dogmatic statements that are open to objection if the full facts are known, and are therefore likely to be somewhat misleading to the inexperienced. Apart from the danger of some of the remarks misleading the tyro it seems redundant because the description of each type of infection contains a paragraph on 'Therapeutics' which gives the best specific treatment available.

The book is a very useful reference book particularly for the specialist in helminthology, but as such its value could be greatly enhanced by correction of errors, some of which have been referred to above. But the cost is high and makes it a luxury for the general practitioner who is only called upon to treat worm diseases as a small part of his work even in countries where this type of infection is prevalent. Such a book as 'Clinical Parasitology' by the author of the volume under review in collaboration with Craig is much better value for the general practitioner because it contains all the essentials in 'Human Helminthology', with protozoology and entomology of medical interest as well.

P. A. M.

**STEDMAN'S PRACTICAL MEDICAL DICTIONARY.**—By Thomas L. Stedman, A.M., M.D., and Stanley Thomas Garber, B.S., M.D. Fourteenth Revised Edition. With Etymologic and Orthographic Rules. 1939. Baillière, Tindall and Cox, London. Pp. xii plus 1303, with 23 plates and numerous illustrations. Price, 37s. 6d.

To the shame of British medical publishing houses, the medical profession in the British Empire has to rely on American medical dictionaries. For the average medical reader, and writer, in Great Britain this is not so serious, as he is usually able to distinguish American spellings and, we hope, to avoid them, for the colonial and 'Empire' reader it is much more serious, as he is often less familiar with the English language and is much more easily led astray, but for

the editor of an English journal published outside Great Britain the circumstance is a tragedy, as he has to spend half his time changing 'hemoglobin' into 'hæmoglobin' and 'sulfate' into 'sulphate', until he finds he has swung the pendulum too far, so that he has to reinstate 'hemiplegia' which his over-enthusiastic staff had changed into 'hæmiplegia'.

In the circumstances, we must be very thankful to American publishers that we have any medical dictionaries at all in the English, or near-English, language, and we certainly owe a special debt of gratitude to Dr. Stedman, who died on 27th May, 1938, at the age of 84; at the time he was actively engaged in preparing the fourteenth edition of this excellent dictionary.

Dr. Stedman wasn't just content to make a comprehensive dictionary; he had a weakness for etymology and one of his avowed objects was the purification of medical etymology. He certainly achieved a degree of 'purification' and apparently this was sufficient to satisfy him for in the eleventh edition of his dictionary he claimed that his purpose had 'been nearly attained'. One of his greatest triumphs was the restoration by the final 'e' to the alkaloids and chemical bases, to distinguish these from glucosides, in the *Journal of the American Medical Association*, and the transformation of the offensive 'k' to the correct 'c' in words derived from the Greek, e.g., *ancylostoma* and *leucæmia*. We cannot help feeling that Dr. Stedman's life must have been a difficult one or his powers of rationalization particularly well developed to be able to strain at such gnats and yet swallow the whole corps of camels that the American language provides.

He explains that the Greek diphthongs *ae* and *oi* become *a* and *o* in Latin and the same, or simply *e*, in English. It is a pity that he hadn't a little more to say on this last point; we should like to have heard how he justified the American practice. Nevertheless, Dr. Stedman with the limitations of his American loyalties was a great scholar, has served medical literature well, and will be missed.

The present volume was largely prepared under his direction. It is well up to the standard of its predecessors. A pleasing innovation is the reproduction in English of the Hippocratic oath as a frontispiece.

**CHRONIC ARTHRITIS.**—By Robert T. Monroe, A.B., M.D. (Reprinted from Oxford Loose-Leaf Medicine). Edited by H. A. Christian, A.M., M.D., LL.D., Sc.D. (Hons.), F.R.C.P. (Hon.). 1939. Oxford University Press, New York and London. Pp. vii plus 84. Price, 8s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

This is a small handbook on the subject of chronic arthritis written by the author primarily for the Oxford Loose-Leaf Medicine from which it has been reprinted. It begins with a foreword written by Dr. Henry A. Christian who considers that as the proportion of older people are increasing the incidence of diseases of the joints is also going up. After describing briefly the anatomy and physiology of joints and their various architectural units, the author has put forward a very simple classification based on structure rather than on etiology. He calls the diseases of the synovia, which are also known as rheumatoid arthritis, atrophic arthritis owing to the prevalence of atrophy and asthenia in such conditions. Diseases of the joint cartilages, which are known as osteoarthritis, have been classed as hypertrophic arthritis and the diseases of the extra-articular supporting tissues as periarticular fibrositis. In dealing with these three types of arthritis the author has traversed a wide field by discussing the relative merits of the different factors in an unbiased manner. For instance, while not overlooking the part played by infective foci in the etiology of atrophic arthritis he has not been a blind faddist but has always kept an open mind. His remark that too many teeth have been sacrificed in the name of infective etiology is very wise. While infection plays an important rôle in the causation of atrophic arthritis the former, according to the author, has no direct bearing on the

hypertrophic type where trauma is the most important etiological factor. The description of the clinical features of the different types of arthritis will be read by everybody with interest and the subject of their management and treatment will be found most comprehensive and of much practical value.

In this connection, the writer has very pertinently commented on the use of some of the drugs and this should be a check to their irrational and indiscriminate use. He goes on to say 'it is fruitless to review the amazingly long list of antirheumatic remedies. Some show ingenuity, as bee venom, histamine and cholin iontophoresis and chaulmoogra oil; others are thoughtlessly conceived as pills of concentrated spinach; many are improper combinations of sedatives, salicylates, laxatives and potentially harmful drugs. They flourish on the gambling spirit of people, who are glad to try their luck on escaping the difficult programme that nature eventually enforces'.

The whole subject has been presented in such a simple and practical manner that this book will be found extremely useful to every practitioner, each and every one of whom has frequently to deal with patients afflicted with this very chronic and painful malady.

M. N. D.

**THE SYNOVIAL MEMBRANE AND THE SYNOVIAL FLUID WITH SPECIAL REFERENCE TO ARTHRITIS AND INJURIES OF THE JOINTS.—By David H. Kling, M.D. Baillière, Tindall and Cox, London. Pp. 283, with 80 illustrations and 34 tables. Price, 25s.**

THIS monograph is based upon the findings of a large amount of original research conducted by the author over a period of fifteen years. His work proves that the old theories regarding the structure and function of the synovial membrane, and the origin and function of the synovial fluid, are inadequate.

A proper study of the synovial membrane reveals that it is not a simple structure throughout; it contains secretory elements in certain areas. These areas produce the normal synovial fluid, which consists chiefly of mucin, by active secretion. This would seem to dispose of the theories which seek to account for the presence of mucin by calling it the interstitial tissue of the synovial cells, produced by their degeneration.

In pathological conditions, effusions consist of the mucin produced by the activity of the secreting cells and also of a transudate or exudate derived, *via* the synovial membrane, from the circulation. There is thus ascribed to the synovial membrane a dual structure and function, and to the fluid a dual origin.

Much of the book is taken up by descriptions of experimental technique and results, and tables of data and other findings. The concluding chapters indicate the clinical applications of all this work, and the reader will find suggestions for routine biochemical and microscopical investigation of joint effusions.

A thoughtful and painstaking book, it is recommended to those interested in the problems of joint conditions, both medical and surgical.

W. McN. N.

**MYTHOLOGY OF THE SOUL: A RESEARCH INTO THE UNCONSCIOUS FROM SCHIZOPHRENIC DREAMS AND DRAWINGS.—By H. G. Baynes, M.B., B.C. (Cantab.). Baillière, Tindall and Cox, London. Pp. xii plus 939. Illustrated. Price, 32s. 6d.**

In his preface the author maintains, and perhaps rightly, that the type of mental disorder now labelled 'Schizophrenia' lies at the very roots of the psyche. Hence, to investigate it, only an introverting psychological method is suitable. The author regards Jung's analytical method as set forth in his 'Psychology of Dementia Præcox' to be the only effective introverting technique in western Europe. To all who have been appalled by the seemingly insoluble riddle of the schizophrenic's mind, the author's view that psychology as a science is deeply bound up with the history of

civilization, of philosophy and of religion and, above all, with primitive mentality, will make a strong appeal. This is also Jung's view. The basic feature of this remarkable book is the study of two patients of the author, one of whom was himself a doctor. The other patient was by profession a draughtsman. Both patients were psychoanalysed but in addition to this, both were encouraged to draw whatever came into their minds. With the exception of the reproduction of three paintings by Paul Klee, a reproduction of the *Lamaist Vajra-Mandala*, and the *Muladhara Chakra* from Avalon's *Serpent Power*, the 53 illustrations are all pictures drawn by the author's two patients. The author is by no means the first individual to trace out the inner experiences of schizophrenics and the same order of experiences in primitive races. Long before the advent of psychoanalysis psychologists were aware of the unexpected light which a study of early psychic stages in evolutionary development threw upon the study of dreams and functional disturbances of thought. The present work goes a long way to confirm the hypothesis that the abnormal process is a primitive process. An ardent disciple of Jung, the author would appear to think that the transformation of the libido as conceived by Jung is sufficient to explain all archaic beliefs, myths, fairy tales and the like. In everyone of the magic archaic experiences are present as the undercurrent of the waking thoughts of the day, but only in specifically schizophrenic types does this undercurrent come to active conflict with the ordinary thoughts of the understanding. In schizophrenia it is more especially the initial states which really bring these archaic magic experiences to flower. The biological revolution of puberty often forces the disease to its first manifestation. In this period of life experiences take place which may plunge the human being into a shoreless maelstrom of uncertainty. Whether to follow his enthusiastic impulses and give himself freely to the world or to withdraw gloomily into the self. This and much more the author describes with meticulous precision. Every student of psychology in any of its branches cannot fail to profit by a study of the fascinating material presented to his inspection.

O. B.-H.

**THE ANATOMY OF THE HUMAN SKELETON.—By J. Ernest Frazer, D.Sc. (Lond.), F.R.C.S. (Eng.). Fourth Edition. 1940. J. and A. Churchill, Limited, London. Pp. viii plus 300, with 219 illustrations, many in colour. Price, 30s.**

THE reason given by the author for the production of the fourth edition of this book is that the modifications in terminology had not been finally decided upon when the third edition was published. In addition, however, certain changes and corrections have been incorporated.

This is not a simple description of the bones such as one is accustomed to find in the typical textbook of anatomy, for although the bones naturally form the basic structure of the book, as they do of the human body, their description is amplified by a full discussion of all the structures with which they come into relation as well as the sites of attachment of muscles, ligaments, etc. The descriptions are clarified by numerous black-and-white drawings and coloured plates in which the various areas on the bones are marked in special colours indicating the attachment of special structures, for example, brown for muscles, blue for synovial membranes, yellow for ligaments and so on. Once this colour scheme has been understood the reader can see at a glance what functions different parts of a bone perform.

It is a book that would be useful for a student, to give him a wider insight into the true function of the skeleton than he is likely to acquire from the ordinary textbook, but we doubt if there are many students who can afford another thirty shillings (twenty rupees) on a book that can never replace but only act as an adjuvant to the standard anatomy he must possess.



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**THE CARE OF YOUNG BABIES.**—By John Gibbons, M.B. (Cambridge), M.R.C.P. (Lond.). 1940. J. and A. Churchill, Limited, London. Pp. ix plus 169, with 8 plates and 5 text-figures. Price, 3s. 6d.

MANY books on the subject of the rearing of infants have been produced in recent years: some good; some indifferent.

This little book is not only in the former category, but is in the highest class, and the author is to be congratulated on the extremely good advice he has laid down for mothers in language which is easily understandable to the lay mind, for the book is in no sense of the word, a medical one per se.

Dr. Gibbons makes reference to many of the 'old wives tales' which were in vogue during the latter part of the last century and the beginning of this one, and disposes of them, in many cases, misleadingly with logical arguments.

He makes reference to the fond grandmamma who so often upsets the careful routine laid down for the infant.

He cites instances where good advice has been flouted, with such firmness, that one may be excused for believing that he would like to have added to the Litany, 'From the stupidity of some mothers, Good Lord deliver us'.

This is a truly excellent booklet which every mother can read with advantage.

**ILLUSTRATIONS OF BANDAGING AND FIRST-AID.**—Compiled by Lois Oakes, S.R.N., D.N. (Leeds and Lond.). 1940. E. and S. Livingstone, Edinburgh. Pp. vii plus 248. Illustrated with 290 photographs. Price, 6s. Postage, 6d.

'It is the aim of this book to enable the student, by means of pictures, to quickly master (Oh, Lois!) the science and art of bandaging and first-aid in fractures and hæmorrhages'. 'For the sake of clarity the operator is not always shown in the position that he would normally occupy in relation to the patient, and, for the same reason, not always holding the bandage exactly as it would be held in the natural circumstances'. We've got you, and the idea is a very sound one, but 'for the sake of clarity' it might have been expressed rather differently.

These two sentences will, we hope, give the reader a line on the scope of the book and on the weakness of the writer's literary style, but we do not honestly think that the latter matters. The photographs are excellent, and, even if a large percentage of the explanatory sentences contain unattached participles, the meanings of such sentences as 'note that the ears are covered up, in applying this bandage' are really quite clear.

There are four sections, triangular bandaging, roller bandaging, first-aid in hæmorrhage, and first-aid in fractures.

It is a book that will be useful to the doctor, the student, the nurse and the 'first-aider', and all those that have to teach them.

**TEXTBOOK OF PUBLIC HEALTH.**—By W. M. Frazer, O.B.E., M.D., Ch.B., M.Sc., D.P.H., and C. O. Stallybrass, M.D. (State Medicine), Ch.B., D.P.H., M.R.C.S., L.R.C.P., Order of St. Sava. Tenth Edition. 1940. E. and S. Livingstone, Edinburgh. Pp. x plus 504. Illustrated. Price, 21s. Postage, 7d.

This tenth edition is practically a new text. It accomplishes fully its stated objective of covering the information required by examining bodies for the English D.P.H. A mine of information has been compressed within the 500 pages. The text possesses the great advantage of having been compiled by authors who are both teachers of a university and at the same time are practitioners of public health administration. It is of interest to note that this textbook began its career in 1874 as 'Medical Police' with subsequent evolution of its title through 'Forensic Medicine and Public Health' to 'Public Health' alone, reflecting the trend of practice. The full accounts provided of the

recently consolidated Public Health (1936), Housing (1936) and Food and Drugs (1938) Acts will be found particularly useful. The chapters on Genetics and Mental Hygiene are somewhat superficial and lack practical indication of their specific utilizability in administration. Also the advice as to site and construction of hospitals, particularly isolation, is not in line with present epidemiological knowledge but conforms to legal requirements that lag very badly in this respect. One trusts that the concluding chapter on Medical Aspects of Civil Air Defence may be required no longer 70 years hence in a textbook of Public Health. Technical description of types of bombs and their action indicates the queer twist given to the trend of public health by world conditions.

The tenth edition can be heartily recommended to anyone desirous of reference to English public health practice. Its value in India lies in furnishing basic information, particularly with respect to the impersonal public health services. In its personal public health, the absence of consideration of particular problems of rural public health would be considered the chief drawback under local conditions.

**BENIGN LYMPHOCYTIC MENINGITIS: (ACUTE ASEPTIC MENINGITIS).**—By Rustom Jal Vakil, M.D. (Lond.), M.R.C.P. (Lond.), D.T.M. & H. (Lond.), F.R.F.P.S.G. 1939. Printed by V. V. Bamardekar at the India Printing Works, Fort, Bombay. Sole Agents:—The Popular Book Depot, Grant Road, Bombay 7. Pp. viii plus 94

This small handbook contains a summary of the work done and clinical features and diagnosis of that little-understood condition acute aseptic meningitis which is also known as benign lymphocytic meningitis. The general medical profession, particularly in India, is not at all familiar with this condition and it is generally labelled as meningism, poliomyelitis, tuberculous meningitis or encephalopathy due to various diseases. A comprehensive description of the disease will therefore be welcome to the profession. The author states that benign lymphocytic meningitis is a definite disease of the central nervous system involving the meninges and is caused by a filter-passing virus which has been identified and isolated. In the blood of infected person and experimentally-inoculated animals, antibodies develop and the demonstration of the latter by protection experiments constitutes an important test for diagnosis of the condition. The writer lays emphasis on the confusion which this condition often causes in the diagnosis, particularly of tuberculous meningitis and he has therefore devoted a special chapter to this subject. He says that while tuberculous meningitis is uniformly fatal, benign lymphocytic meningitis has always a favourable prognosis. At the end of the book, there are records of five English cases and two Indian cases. A very exhaustive bibliography is also appended and this will be of great help to anybody who may be interested in the disease.

The two Indian cases reported by the author are not very convincing and certainly one of them has been diagnosed purely on clinical grounds even without the help of the lumbar puncture. In this respect Dr. Vakil cannot be considered to have escaped the errors of a general practitioner although, of course, he has suggested benign lymphocytic meningitis.

The book is an excellent critical review of benign lymphocytic meningitis and should be read by every practitioner in India.

M. N. D.

**HYGIENE FOR NURSES.**—By John Guy, M.D., D.P.H. (Camb.), F.R.F.P. & S. (Glas.), F.R.C.P. (Edn.), and G. J. I. Linklater, O.B.E., M.D., D.P.H., D.T.M. & H., M.R.C.P. (Edin.). Fifth Edition. 1940. E. and S. Livingstone, Edinburgh. Pp. xlii plus 239. Illustrated. Price, 5s. Postage, 5d.

This subject is too often rendered dull and tedious to nurses by much superfluous subject-matter. The

authors have avoided this pitfall, and the book makes interesting reading, besides supplying all the knowledge that the nurse in training requires for practical purposes and examination, in hygiene and dietetics.

**HEALTH BULLETIN, NO. 14. MALARIA BUREAU, NO. 6. 'HOW TO DO A MALARIA SURVEY.'**—By Colonel Sir S. R. Christophers, F.R.S., I.M.S. (Retd.), Lieut.-Colonel J. A. Sinton, M.D., D.Sc., I.M.S. (Retd.), and Lieut.-Colonel G. Covell, M.D., D.P.H., I.M.S. Fourth Edition revised by Lieut.-Colonel G. Covell, I.M.S., Director, Malaria Institute of India. 1939. Published by Manager of Publications, Delhi. Pp. vi plus 208. Illustrated. Price, Re. 1-12 or 2s. 6d.

THIS was one of the earliest publications of the Malaria Survey of India. It has proved invaluable to malariologists in India and abroad. The present, the fourth edition, has been revised by Colonel Covell.

It is well illustrated by line drawings throughout and there are invaluable tips to help the malarial surveyor not only to carry out the various procedures but to do them rapidly and accurately.

It is a low-priced publication and every malariologist in India should possess a copy.

**HEALTH BULLETIN NO. 6. MALARIA BUREAU NO. 1. 'LECTURES ON MALARIA.'**—By Lieut.-Colonel G. Covell, M.D., D.P.H., I.M.S. 1940. Published by the Manager of Publications, Delhi. Pp. 33. Price, As. 5 or 6d.

THERE appears to be a real need for a bulletin containing rather more detailed information regarding malaria, to meet the requirements of officials and others who are not necessarily medical men, but whose duties constantly bring them into contact with the manifestations of the disease, such as engineers, forest officers, members of the Indian Civil Service, officers of the defence services, railway officers, managers of tea, coffee and rubber estates and of other industrial concerns. Although such individuals may already possess some knowledge of the basic facts concerning malaria, this is often incomplete, and they are usually most anxious to learn more about the subject.

The lectures included in this bulletin are designed to afford the type of information likely to be most generally useful in the above-mentioned circumstances, and to supply answers to the questions which experience has shown are most frequently asked.

Though not primarily written for the medical man, there are few doctors who will not learn a great deal from these lectures. They are both encouraging and inspiring. We recommend them very strongly to the general medical reader as well as to the malariologist.

**MEDICAL RESEARCH COUNCIL. SPECIAL REPORT SERIES, NO. 235. 'THE CHEMICAL COMPOSITION OF FOODS.'**—By R. A. McCance and E. M. Widdowson. 1940. Published by His Majesty's Stationery Office, London. Pp. 150. Price, 4s.

THE nutritional and dietetic treatment of disease, as well as research into problems of human nutrition, demand an exact knowledge of the chemical composition of food. The pioneering investigations into food chemistry were made in Germany and the United States of America, and until after the war of 1914-18 this country lagged far behind. The researches on vitamins which began to make rapid progress soon after the war, and in which this country played a leading part, stimulated a demand for a wider knowledge about human foods. Accordingly, when Dr. McCance approached the Council for support in order that he might determine, in the first instance, the amount of carbohydrate in foods used in the treatment of diabetes, it was recognized that the project was likely to have practical importance, and a grant was made for work along these lines at King's College Hospital, London. For twelve years the Council have continued to support similar and related studies by Dr. McCance and his colleagues, first at King's College Hospital and latterly

at the Department of Medicine, University of Cambridge; and during that time the investigators have gradually extended the scope of their inquiries. A system of analysis has been evolved by which they have determined all the important organic and mineral constituents of foods, with the exception of the vitamins, which have formed the subjects of extensive research by other workers and by different methods. Some idea of the amount of detailed analytical work involved in these chemical studies may be gathered from the statement that as many as twenty different constituents may require to be determined in a single foodstuff.

This systematized analytical procedure has now been applied by Dr. McCance and his colleagues to almost all the foods commonly eaten in Great Britain. The method of approach has been somewhat different from that of previous workers in the same field; for the foods have been analysed, not only in the raw state, but also as prepared for the table, and studies have been made of the losses introduced by cooking. The investigators have also examined the question whether all the constituents of a food are really available for the body's use; whether they are decomposed in the alimentary canal, or fail to be absorbed. Some of the analytical data have already appeared in earlier reports in this series, and the present volume includes previously published figures—which have been carefully checked and corrected where necessary—as well as many others which are new. It should thus contain all the quantitative data likely to be required for practical work involving detailed knowledge of the chemical composition of British foods. It cannot, however, be regarded as completely superseding the three previous reports, for the latter contained much information which has not been reprinted.

An unusual feature in this report is the inclusion of about one hundred recipes of common English dishes, including both the ingredients and a short description of how they are prepared. This will serve the double purpose of helping the physician to calculate the value of a diet of which these mixed dishes form a part, or conversely of helping the nurse or patient to work out an appetizing diet along the lines prescribed by the physician. These recipes are cleverly selected from standard cookery books by Miss C. M. Verdon-Roe.

It is a book which will be of very great value to the Indian worker, particularly if he uses it in conjunction with his *Health Bulletin No. 23* which supplies the analyses of foods that are peculiarly Indian in origin.

## Abstracts from Reports

### ANNUAL REPORT OF THE MYSORE STATE DEPARTMENT OF PUBLIC HEALTH FOR 1938.

EXCEPT for a rise in the incidence of plague, public health was generally satisfactory. Five thousand, one hundred and ninety-six deaths from plague were reported during the year against 4,812 in the previous year. In connection with the control of plague, in addition to the anti-plague inoculation and disinfection of houses, cyano-gas fumigation was recommended for adoption in various places. Six thousand, two hundred and eighty-four houses were cyano-gassed, 2,874 in the Kolar Gold Field Sanitary Board area, 100 in the Bangalore City and 3,310 in other places. Eight hundred and eighty deaths from cholera occurred during the year against 4,239 in the previous year. During the year, 789 deaths from smallpox were reported against 1,095 in the previous year. The number of vaccinations was 250,780.

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The total number of births during the year was 150,410 (146,737), the computed birth rate being 22.0 per mille of population as compared with 21.6 in the preceding year. The total number of deaths was 102,228 (102,118) giving a death rate of 14.9 per 1,000 of population as against 15.1 in the previous year. The total number of deaths among children under one year of age was 16,082 (15,567) giving an infant mortality rate of 106.9 against 106.1 in the previous year.

Experimental work was continued in order to determine the standards of purity of most of the common articles of food with reference to their nutritional value. As a result thereof, action was taken to discourage the use of polished rice and to encourage the use of hand-pounded rice. Experiments on other articles of food are being conducted.

During the year, 190 cinema shows were arranged in different places in the districts. Two health exhibitions were held, one at the Annual Dasara Exhibition at Mysore, where a large section on nutrition and its importance was newly added and the other at Hassan in connection with the State Women's Conference.

The health centre at Closepet continued to do good work. Village improvement work was started by the health league in 18 new villages. Improvements were effected to several houses by providing latrines, soak pits, manure pits, and windows and by plastering and white-washing them.

**Malaria control.**—Control of malaria is a very important public health problem in the State as malaria accounts for over 30 per cent of the total mortality. Control work was continued in the cities of Bangalore and Mysore and in Hiriyur, Mudgere, Nagenahalli, Mandya and ten selected villages in the Irwin Canal area. It was started in Chikmagalur and Sakrepatna also. Malaria survey was completed in Shimshapura, Belur, Jog and Devarayasamudram and in ten villages in the Marconahalli area, 17 villages in the Closepet area and two villages close to Bangalore as well as in the Alageshwar tea estates, the area around the Princess Krishnammanni Sanatorium, Mysore and Balehalli village near Chikmagalur. The annual spleen and parasite survey of the Bangalore and Mysore was done, as usual. The spleen rate for Bangalore was found to be 0.13 as against 0.31 in the previous year and the parasite rate 0.91 against 0.5. The spleen and parasite rates for Mysore city were 1.3 and 2.2 per cent against 2.6 and 7.2 in the previous year. Both malarial and Paris green were used as larvicides. The effects of malaria engineering measures were observed during the year in the three villages.

The guinea-worm staff visited 960 villages during the year, 524 step wells were examined and 66 wells were newly stocked with fish. The larvicidal fish was renewed in 111 wells, and 19 wells were treated with perchloron.

The staff on hook-worm control carried on the work of propaganda and the construction of bore-hole latrines, in the villages where infection was found to be heavy. They visited 1,539 houses in 38 villages. One hundred and thirty bore-hole latrines were constructed during the year.

In addition to the work on water-supply scheme at Mysore, Bethamangala, Kolar, Hiriyur, Harihar, Shimoga, Sagar, Saklespur, Shikarpur and Hassan, 14 towns and villages were provided with protected water-supply.

Plans for the improved lay out of five places and type designs of slaughter-houses, mutton stalls and rat-proof dwelling houses were prepared during the year.

ANNUAL PUBLIC HEALTH REPORT OF THE PROVINCE OF ASSAM FOR THE YEAR 1938. BY LIEUT.-COLONEL A. M. V. HESTERLOW, M.B., Ch.B. (EDIN.), B.Sc., P.H. (EDIN.), D.T.M. & H. (EDIN.), I.M.S., DIRECTOR

THE death rate for the year 1938 was higher than the decennial average by 2.77. A noticeable increase was recorded in the number of deaths from cholera (6,465).

The increase in the number of deaths from cholera was the principal factor in raising the death rate in 1938.

Diseases	1938	1928-37
Cholera .. ..	1.50	0.70
Smallpox .. ..	0.21	0.21
Plague .. ..	.. ..	.. ..
Fevers .. ..	13.33	12.27
Dysentery and diarrhoea .. ..	1.50	1.23
Respiratory diseases .. ..	0.87	0.76
Injuries .. ..	0.25	0.25
All other causes .. ..	4.75	4.22
<b>TOTAL .. ..</b>	<b>22.44</b>	<b>19.65</b>

Nine hundred and seventy-two thousand, six hundred and ninety-six persons were inoculated with cholera vaccine excluding those inoculated in tea estates. Four hundred and ninety-five thousand, eight hundred and seventy-two doses of bacteriophage were issued during the year under report. As in past year, seven mobile epidemic units, each consisting of three sub-assistant surgeons and six disinfectant carriers, were employed; this staff was found inadequate. When there is a severe epidemic which breaks out in several districts simultaneously, affecting extensive areas where communication is not good, it becomes impossible for the staff to cover the whole area. It was for this reason and to make the unit more useful that it is now customary to designate as the epidemic unit—a unit consisting of one sub-assistant surgeon and two disinfectant carriers and to post these in suitable centres in the district from which infected areas would be more readily accessible, instead of locating them all at district headquarters. In such circumstances, the only alternative is to close the Public Health dispensaries and to utilize the staff for epidemic duty, dislocating the system of kala-azar treatment work, which is very undesirable. Additional units are therefore imperative.

One hundred and fifty deaths from cholera were reported from tea estates during the year compared with 220 deaths in 1937. The corresponding ratio per mille being 0.12 and 0.22 respectively.

A total of 618 villages was infected with smallpox. Mortality from smallpox was reported from 67 out of 148 registration circles. The highest number of deaths (280) was recorded in May and the lowest (46) in September.

No case of plague was reported.

Fevers were responsible for 59.46 per cent of the total provincial mortality as compared with 62.13 per cent in the previous year. These figures include deaths from malaria, kala-azar and also from various other diseases, which have fever as their predominant symptom.

Two hundred and thirty-five deaths from cerebro-spinal fever were reported from three districts.

Three thousand, two hundred and thirty-four cases of yaws were treated against 2,607 in 1937. In each of the districts of Goalpara and Nowgong, three more centres undertook the treatment of yaws. Two sub-assistant surgeons received training in the diagnosis and treatment of yaws in each of the districts of Kamrup and Nowgong. The treatment with neosalvarsan has proved very successful.

Twenty-five cases of naga-sore were treated in the Kamrup district during the year under report against 73 in 1937.

The number of deaths from kala-azar was greater in 1938 by 281 than that of the preceding year. The number of patients treated was larger by 5,217. The increase in deaths is shared by the districts of Sylhet, Kamrup and Sibsagar and the increase of cases treated



is shared by all districts. The method of diagnosis and treatment of kala-azar was the same as in previous years. Neo-stibosan is again being used in urban areas only at the discretion of the medical officers. The price of this drug has now been reduced.

In Cachar district 422 villages were surveyed and 331 suspected cases were discovered of which 104 were found to be positive. All these cases were brought under treatment.

Two kala-azar treatment centres, one at Ratanpur and the other at Matijuri in the Hailakandi subdivision, were opened during the year under review.

Four thousand, three hundred and seventy-five lepers received treatment in the leper asylums and other centres of treatment under the Medical and Public Health Departments during the year under review. Of these 910 lepers were treated in the leper asylums, wards and colonies.

#### SEVENTY-SEVENTH ANNUAL REPORT OF THE GOVERNMENT CINCHONA PLANTATIONS AND FACTORY IN BENGAL FOR THE YEAR 1938-39

TOWARDS the middle of the year under review the convention price of quinine sulphate rose by 1d. per ounce due chiefly to a continued fall in the value of sterling. Government prices, however, remained steady throughout the year. An examination of recent import figures reveals an interesting feature, namely, that the Indian quinine trade has been gradually passing from the Dutch and the British into the hands of the Germans. This is undoubtedly due to the system of subsidized exports that has prevailed in Germany. The bark, of course, still comes mainly from Dutch sources in Java.

Mr. Wilson's enquiry into the prospects of cinchona cultivation in India, referred to in our last report, was completed during the year. His report gives a brief account of the recent trend of development of cinchona cultivation in India, both through Government and private enterprise, and shows that, taking India as a whole, there has been little progress towards reducing the margin between the country's total consumption of quinine and its production. On the findings of the report the scope for future development in cinchona lies mainly in the south of India. This may be explained by the fact that the whole table-land of the Deccan offers suitable ranges of elevation, while in the north, the elevations are to be found only along a narrow belt at the foothills of the Himalayas and its offshoots.

The report brings out in striking manner the paucity of quantitative data on cinchona cultivation in India. Neither the yield tables nor the cost figures given by Mr. Wilson can be taken as authentic. They have not been derived from statistical averages, but are based on general experience. They give, nevertheless, useful indications which should be of help towards formulating schemes of extension in new areas, where no experimental work has yet been done. The need for well organized quantitative data is being increasingly felt in the Bengal Cinchona Department in connection with the planning of production and distribution. The present system of plantation mensuration which was devised nearly thirty years ago has completely broken down under the altered methods of cultivation and harvesting.

The soil studies in connection with the Wilson enquiry give interesting generalizations in the field of which little is yet known to us. The results must, however, be accepted only on a tentative basis and before a proper correlation can be established between soil factors and the growth of cinchona, more comprehensive schemes of sampling must be devised to eliminate the climatic and inheritance factors. Further soil studies on an extensive scale are desirable not only to find the characteristics best suited to cinchona, but also with

a view to devising methods of maintaining these characteristics over a series of planting cycles. This is one of the really pressing problems of cinchona cultivation in India, because of the rigorous climatic and topographic conditions in which cinchona has generally to be grown in this country.

Mr. Wilson stands on undisputed ground when he stresses the need for research. This need has been previously mentioned in our own reports. There is on the one hand room for improvement in our present methods of selection, propagation, cultivation and harvesting. On the other hand it is necessary to place even the existing methods on a scientific basis, so that they may depend for successful exploitation not so much on that empirical experience, which is known as the personal touch, as on the observance of principles established by experiment which take into account the varying conditions of locality and time. The successful cultivation of cinchona is no doubt an art, but it is an art that, to obtain perfection, must take the fullest advantage of existing knowledge.

#### REPORT OF THE MEDICAL RESEARCH COUNCIL, LONDON, FOR THE YEAR 1938-39

##### MEDICAL RESEARCH AND THE WAR

DURING the past year the work of the Medical Research Council has gone steadily forward and, except in the case of their administrative staff, the continuous state of war expectancy affected it but little until the late summer. The policy of the council has been to encourage their research staff and grantees to continue their investigations as under normal conditions. On the outbreak of war this policy has been maintained, although some research workers have had to respond to special calls—to join the defence services, to take part in emergency schemes, or to undertake special investigations suggested by war conditions.

It cannot be denied that the disturbed political atmosphere of the past year has brought increased difficulties to those whose work depends so greatly upon concentration of thought and action, and upon freedom from worry. At the same time, perusal of this Annual Report, and especially the account of the work done at the National Institute for Medical Research and at other special centres throughout the country, will show that a harvest of discovery has been procured in spite of the unrestful situation.

The council foresaw that the work at the National Institute would be at least as important in time of war as in time of peace, and took action to provide protection for the staff at Hampstead. Since the outbreak of hostilities, therefore, the staff of the National Institute have been able to proceed with their work. It cannot be expected, however, that medical research either there or elsewhere can remain unaffected by war. Apart from changes and possibly some reduction in personnel, the natural desire of many investigators is to leave their peace-time problems and direct their attention to subjects of immediate war interest. The presentation of new war problems requiring investigation is therefore usually received with enthusiasm by the research worker. The danger, in fact, is not that of failure to investigate such problems but rather that, by switching over to other objectives of immediate practical interest, the fruits of promising research unrelated to war should be lost. It is the intention of the council, so far as they are able, to prevent such losses to important knowledge.

At the same time, it is recognized that war conditions in themselves offer special opportunities for the acquisition of knowledge which is by no means of emergency interest only. It will be remembered, for instance, that the Medical Research Council (then Committee) came into being immediately before the last war, and during their early years directed most of their attention and energy to the solution of problems presented and made urgent by the emergency. In the words of the Annual Report for 1917-18, 'the needs of war have given stimulus to enquiries upon many





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sides, and out of the circumstances of the time some unusual opportunities and facilities have come to scientific workers'. The history of work done during the years 1914-18 is a remarkable one, and a perusal of the records of the Medical Research Committee of those years cannot but excite admiration both for the success with which the opportunities offered were seized by workers in this field and for the inspiring energy with which the Secretary, Sir Walter Fletcher, carried out the general policy. It was the first time in the history of this country that organized scientific endeavour in medical research ever had a chance of justifying itself, and right well did it respond.

It will be asked what contribution medical investigation can make in the present war. It is at least certain that the more recent developments of blood transfusion, together with a well-organized service for allowing this to be carried out on a large scale, will lead to results far better than those obtained by the transfusion of gum acacia solution introduced in the later part of the war of 1914-18 through the work of the Committee on Shock.

In the case of wound infection, probably the largest single cause of death among wounded men reaching hospital in the last war, it can be safely predicted that modern discovery in the chemotherapeutic treatment of bacterial infection will be one of the outstanding beneficial factors. Where the infection is due to hæmolytic streptococci, it may be hoped that the established curative effect of the sulphanilamide group of compounds will be as successful in wounded men as it has proved in puerperal sepsis and septicæmia. The evidence of the curative effect of these compounds in gas-gangrene infection is not so certain, but what evidence there is suggests that in this case also they will be life saving. It will be necessary as soon as possible to get evidence on this point, and especially to evaluate the relative curative effects of the sulphanilamide compounds and gas-gangrene antitoxin. Although the use of gas-gangrene antitoxin still receives wide support, its beneficial effects have never been established with certainty. Needless to say, however useful the new chemotherapeutic compounds will prove, it is not likely that the need for proper surgery in the treatment of wounds will diminish.

Another matter which presses for early solution is the possible prophylactic effects of the sulphanilamide derivatives, apart from their curative action. Arrangements have already been made by the Army Medical Service to determine whether the administration of these compounds immediately following injury will prevent subsequent infection by the more common pathogenic micro-organisms.

#### WAR EMERGENCY SERVICES

During the two years preceding the war the Medical Research Council were entrusted with a number of responsibilities, on behalf of H. M. Government, for the preparation of various emergency medical services.

#### Medical supplies

One of the first things of the kind which the council were asked to undertake was the organization and supply of certain antitoxins to be held in readiness for war purposes.

#### Specialist personnel

The ordinary work of the council places them in a unique position as regards contact with those who have special knowledge of different branches of medical science and allied subjects. They have thus, both before and since the outbreak of war, been able to assist in finding men possessing the highly specialized qualifications required for various items of emergency work which have arisen.

#### Blood transfusion depôts

The council also undertook the organization of four depôts for the collection, storage and supply of blood for transfusion purposes. These are situated in the home counties and are intended—in addition to serving their own immediate neighbourhoods—to augment the arrangements made by the hospitals in London itself.

#### Nutrition in time of war

During the last war knowledge of human nutrition which was then new proved to be of great value in dealing with questions of the nation's food supply under conditions of restriction. It is no less vital that this knowledge should be applied now, if similar conditions recur.

#### Research on war problems

Some of the medical problems presented by the war are old ones for which no complete solution had been found. Among these is the question of shock occurring after serious wounds or severe operations. The council have appointed a special committee to review this problem in the light of present-day knowledge, and to organize both laboratory and clinical studies in the subject. Related to this is the question of blood transfusion, with regard to which various investigations are in progress.

Other subjects have taken on fresh aspects under changed conditions. For example, the physiological problems of aviation present themselves in new forms in relation to the flying of modern war machines. In this field the council have been assisting the Royal Air Force, and their secretary is chairman of the special committee set up by the Air Ministry.

#### Virus diseases

*Influenza: epidemic studies.*—Dr. Stuart-Harris, working in association with the institute, studied the clinical conditions in a number of successive outbreaks, and collected material from representative cases for laboratory investigation. Even with material from typical cases, all attempts to transmit a virus infection to ferrets and mice were unsuccessful in the early stages, and it was not until the middle of February that evidence of a connection of influenza virus with the outbreak was obtained. From that time onwards the virus was recovered from a proportion of the cases in each outbreak visited; and additional cases gave evidence of its presence in the increase of neutralizing antibodies observed in samples of blood serum taken during and after the attack.

Altogether, of the throat-washings obtained from different outbreaks only 7, out of 59 tested, yielded virus infecting ferrets. Some of these strains appeared to be of low virulence for the test animals, though all showed antigenic relationship with some of the strains obtained in the more typical epidemics of earlier years.

*Dimensions and properties of viruses.*—In collaboration with Dr. T. F. McNair Scott at the Wellcome Research Institution, Dr. Elford has applied his methods of ultrafiltration and differential centrifugation to determining the dimensions of the infective units of lymphocytic chorio-meningitis; this is a virus disease affecting the brain membranes of mice, and has in more than one laboratory been accidentally found to be transmissible to man. The diameters of the units, as determined by these independent methods, showed excellent agreement, the calculated average values being 50 and 46 millimicrons respectively (a millimicron being a millionth of a millimetre).

#### Immunology

*Reversed anaphylaxis.*—Dr. van den Ende has completed an investigation, which he had undertaken at Cambridge, on the phenomenon termed 'reversed anaphylaxis'. It was known that if an antiserum to guinea-pig serum was prepared by a course of injections into a rabbit, the serum of the immunized rabbit evoked in a normal guinea-pig a train of symptoms closely resembling that observed in the ordinary anaphylactic shock. The completion of the experiments has been deferred by the incidental discovery that the antibody globulin, from the serum of a rabbit immunized against pneumococcus (type I), is a distinct antigen from the corresponding globulin of normal rabbit's serum—a point of interest at least as great as that which led to the experiment.

*Tissue fixation of antibodies.*—A further technical advance has been made in the method, by the discovery

that the sensitizing fixation of antibodies—producing a condition of passive anaphylaxis—does not require the maintenance of the organ in a state of physiological activity at body temperature.

**Bacterial antigens.**—Dr. Elford has initiated a physico-chemical study of the molecular dimensions of these antigens, and of the polysaccharide haptens which can be dissociated from them.

#### Leprosy

Sir Patrick Laidlaw has made experiments which have an interesting bearing on the relation between human leprosy and that occurring in the rat. The rat disease, which is caused by an organism very similar to that found in the leprosy lesions of man, is relatively rapid in development and is transmitted without difficulty from rat to rat; but there was only one previous record of a successful attempt to transmit leprosy to the rat by material from a case of leprosy in man. During the past year material from cases of human leprosy in the Belgian Congo had been sent by air mail to Dr. A. Dubois of Antwerp, and this had been used to inoculate Syrian hamsters.

With this material Sir Patrick Laidlaw found it remarkably easy to transfer a rapidly spreading infection not only to hamsters but the readiness with which the infection was transmitted to rats as well as hamsters, and the observations made on the tissues of these animals after death, suggested to Sir Patrick Laidlaw that the human lesions from which the material was originally obtained were due to infection with the organism of rat leprosy, and not with the organism of the usual human type. This opinion has been confirmed by Dr. Dubois and also by Professor Adler, to whom microscopic preparations and descriptions of the findings were submitted.

With regard to the infection of hamsters with the bacillus of typical human leprosy, it is important to distinguish mere survival of organisms at the site of inoculation from active multiplication and infective

spread to other tissues. Sir Patrick Laidlaw has accordingly studied the behaviour of a number of other mycobacteria. Such organisms differ from true leprosy bacilli in being capable of growth on artificial media. In most cases they could be recovered from the sites of inoculation in hamsters as long as six months after injection; but the survival was strictly local, no organisms being found in the lymph glands, spleen, liver, or other organs. A mycobacterium obtained from butter survived for months in this restricted manner, as well as those which had originally been found in association with leprosy lesions.

#### Protistology

By the methods which had already proved so fruitful in the study of the life-cycles of *Entamoeba histolytica* and *Entamoeba coli*, Mr. Dobell has now worked out a large part of the life-cycle of *Endolimax nana*. He has made further progress with the study of the intestinal flagellates of these hosts, and the knowledge of them required for practical purposes is now nearly complete. Attention has also been given to the flagellate commonly found in the human mouth, with a view to deciding the proper nomenclature of this organism.

[These are a few abstracts from this interesting and valuable report which is all we are unfortunately able to find space for. Important work has also been done on chemotherapy and endocrinology and many other subjects. Apart from the amount of information obtained in this report the list of 37 special committees at the end indicates the wide scope the activities of the Medical Research Council covers. All research workers should have a copy as from it they may gain ideas for lines of their own researches or, on the other hand, be prevented from overlapping in work that is being efficiently pursued elsewhere. It is published by His Majesty's Stationery office and the price is three shillings.—EDITOR, I. M. G.]

## Correspondence

### ROUTINE TREATMENT OF EPILEPSY, WITH SNAKE VENOM

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—Cobra and Russell viper venoms are used together in the treatment of epilepsy. The former acts as an anticonvulsant drug, and also probably reduces sensitivity of the higher centres to extraordinary incoming impulses. Russell viper venom appears to alter the mineral and water metabolism and thus influences the epileptic convulsions. In addition to this, extract of *Rauwolfia serpentina* is added to the venom therapy since it is a good nerve sedative, hypnotic and lowers blood pressure, and thus lowers cerebral excitability. The treatment may be detailed briefly as follows:—

#### ROUTINE TREATMENT OF EPILEPSY WITH VENOMS

##### Drugs to be used:—

- (1) Cobra venom 1 to 10 mouse units (m. u.).
- (2) Russell viper venom 2 to 20 mouse units.
- (3) Extract *Rauwolfia serpentina* 10 to 30 drops in water, twice daily.

##### Treatment:—

Intramuscular bi-weekly injections of cobra and Russell viper venom, mixed together in the following doses:—

- Dose no. 1. Cobra venom 1 m. u. and Russell venom 2 m. u.
- Dose no. 2. Cobra venom 2 m. u. and Russell venom 4 m. u.
- Dose no. 3. Cobra venom 3 m. u. and Russell venom 6 m. u.

So on till 10 doses are administered. Rest for one month and repeat the above course again.

Three to four such courses to be completed, later on one course every six months.

Record of the fits, the dates of occurrence and duration of fits to be recorded, regularly, throughout the treatment.

#### Extract *Rauwolfia serpentina*:—

Ten to thirty drops to be given in an ounce of water at bedtime and early morning or when the fits are anticipated. Doses of rauwolfia and venom may be regulated according to the local and general reaction and according to the response of the patient.

#### *Bromides and luminal*:—

These may be given in the beginning to control the fits, and the latter drug if fits are very frequent and severe in type. Dilantin Sodium Kapsels (Parke, Davis & Co.) is another good drug worth trying. It has been reported to have given encouraging results and is preferable to luminal.

A paper on the above treatment as employed at the School of Tropical Medicine, Calcutta, was read in the Physiological Society in January 1940.

Yours, etc.,

J. S. CHOWHAN,

M.B., B.S., CAPTAIN, A.I.R.O.

Biochemical Standardization Laboratory,  
All-India Institute of Hygiene and Public Health.

CALCUTTA,  
23rd March, 1940.

# The Influence of Virol on the Growth of Children

*A Summary of Investigations\* published in the  
"Medical Officer," March 30 and April 6, 1935*

A NUMBER of children, all receiving their customary home diet, were given either No Supplement, Cod Liver Oil, Halibut Liver Oil (with milk to provide equal calories) or Virol. The experimental scheme provided that each child should have a period on each treatment in turn, in such a way that every possible sequence was included. Rigid statistical control was thus possible.

## Gain or Loss in Weight on Various Supplements :—

Supplement	Total gain in ozs. over all periods	Average gain per child per week in ozs. over all periods	Total loss in ozs. during summer period only	Average loss per child per week in ozs. during summer period only
No Supplement - -	88	0.3	— 103	— 1.4
Cod Liver Oil - -	287	1.0	— 77	— 1.1
Halibut Liver Oil with milk - - - -	333	1.2	— 184	— 2.6
VIROL - - - -	762	2.6	— 7	— 0.1

Whereas earlier investigations had shown that the mere addition of vitamins had no effect on growth, these investigations have conclusively proved that Virol—a balanced food containing all the necessary vitamins—has a definite and remarkable effect in bringing the rate of growth up to the recommended standard. Virol was the only one of the supplements used that promoted this ideal rate of growth.

Virol was the one and only preparation that maintained the children's weight in the hot weather.

\* The full report will be sent on application to Messrs. A. H. Wheeler & Co.,  
Sudama House, Wittet Road, Ballard Estate, Bombay.

# ST. BARTHOLOMEW'S HOSPITAL OPERATION TABLE

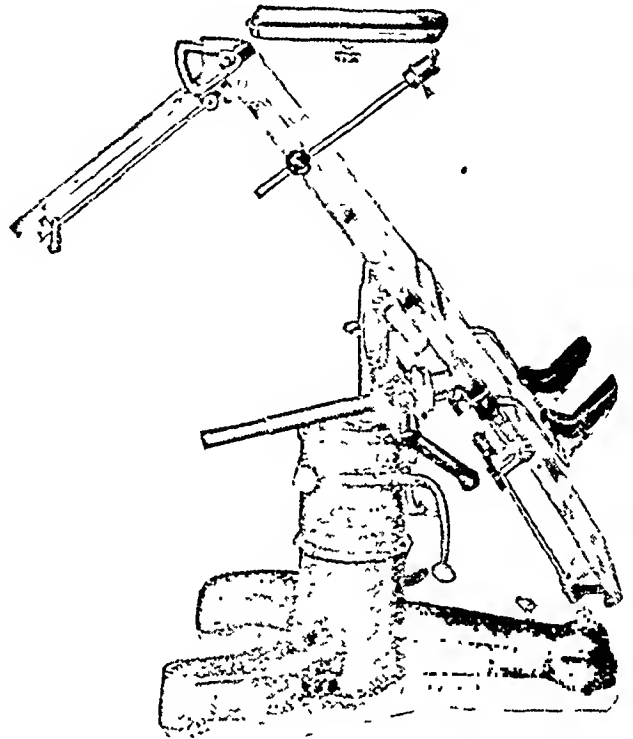
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Easy to operate Release Lever for lowering the table; Trendelenburg position increased to 55° tilt; Foot operated rubber-covered Floor Brake.

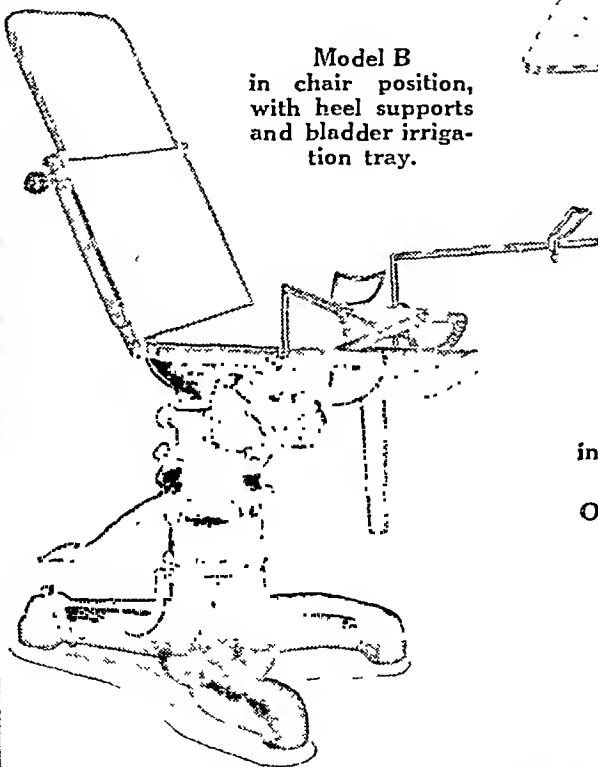
The St. Bartholomew's Hospital Operation Table is now manufactured in five different models and thus supplies a range of modern operation tables embodying the latest ideas of well-known surgeons for carrying out surgical operations.

All models can be supplied with either tripod or platform base.

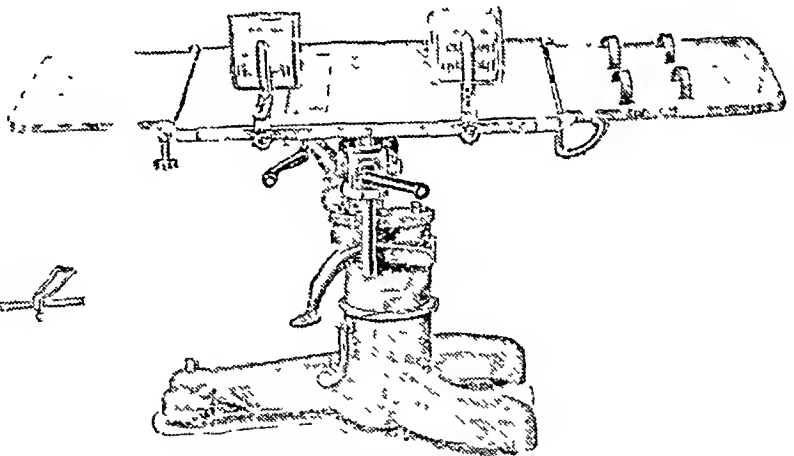


Model A

In Trendelenburg position, 55° tilt, showing shoulder rests and instrument tray in position.



Model B  
in chair position,  
with heel supports  
and bladder irriga-  
tion tray.



Model AC

in lateral position, with back elevator and lateral supports.

Over 1075 of these tables are in use at home and abroad.

*A descriptive booklet, fully illustrated, will be sent on request.*

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## Service Notes

### APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL E. COTTER is confirmed in the appointment of Public Health Commissioner with the Government of India, with effect from the 30th August, 1939.

Lieutenant-Colonel W. J. Webster, M.C., Assistant Director, Central Research Institute, Kasauli, is appointed to officiate as Director of that Institute, *vice* Colonel J. Taylor, granted leave.

On transfer from Ferozepur, Lieutenant-Colonel K. R. Batra assumed charge of the Office of Civil Surgeon, Jullundur, on the forenoon of the 6th April, 1940.

On transfer from Jullundur, Lieutenant-Colonel Jamal-ud-Din assumed charge of the Office of Civil Surgeon, Rawalpindi, on the afternoon of the 12th April, 1940.

On transfer from Montgomery, Major P. C. Dutta assumed charge of the Office of Civil Surgeon, Ferozepur, on the forenoon of the 22nd April, 1940.

On transfer from Campbellpur, Major B. Temple-Raston assumed charge of the Office of Civil Surgeon, Dalhousie, on the 30th April, 1940.

Captain R. I. Reid is confirmed as Deputy Assistant Director-General (Medical Stores), with effect from the 28th February, 1940.

Captain C. L. Greening, an officer of the Medical Research Department, is appointed to officiate as Assistant Director, Central Research Institute, Kasauli, *vice* Lieutenant-Colonel W. J. Webster.

Captain H. A. Ledgard is appointed to officiate as an Agency Surgeon, with effect from the forenoon of the 1st April, 1940, and is posted as Residency Surgeon, Kashmir, with effect from the same date.

Captain F. W. Allinson, Civil Surgeon, Bakargani, on relief, is appointed to act as First Resident Medical Officer, Presidency General Hospital, Calcutta, *vice* Captain W. McN. Niblock.

Captain F. W. Allinson made over charge of the Barisal Jail to Dr. N. Das, on the afternoon of the 9th April, 1940.

Captain J. White, Civil Surgeon, Midnapore, is appointed to act as Superintendent of the Midnapore Central Jail, in addition to his own duties, *vice* Major B. Chaudhuri, with effect from the date on which the latter relinquishes charge of that jail to join the military.

Captain D. W. Taylor, Civil Surgeon, Dalhousie, has been recalled for military duty and made over charge of his duties at Dalhousie, on the 30th April, 1940.

Captain F. V. Stonham, Civil Surgeon, Sargodha, has been recalled for military duty.

### LEAVE

Colonel J. Taylor, C.I.E., D.S.O., K.H.S., Director, Central Research Institute, Kasauli, is granted leave on average pay for 1 month and 26 days combined with leave on half-average pay for 5 days, with effect from the 15th April, 1940.

Major W. Aitchison, Civil Surgeon, on 6 months' leave *ex-India* on Medical Certificate from 12th April, 1940, in continuation of 17 days' leave in India from 26th March, 1940, with permission to prefix the Easter and the Holi holidays from 22nd to 25th March, 1940.

Major M. K. Afridi, Assistant Director, Malaria Institute of India, is granted leave on average pay for 1 month, with effect from the 22nd April, 1940.

Major G. F. Taylor, Professor of Clinical Medicine, K. E. Medical College, Lahore, made over charge of his duties on the 21st April, 1940, and proceeded to England as medical attendant to Mr. D. Gainsford, I.R. He will be treated on 3 months' leave from the date he reaches England.

Captain W. McN. Niblock, First Resident Medical Officer, Presidency General Hospital, Calcutta, is granted leave, with effect from the date on which he is relieved.

### PROMOTION

Lieutenant-Colonel N. S. Jatar, C.I.E., D.S.O., Inspector-General of Civil Hospitals and Inspector-General of Prisons, C. P. and Berar, has been advanced to the higher position of his rank, *i.e.*, to the rank of Lieutenant-Colonel, selected for increased pay for ability and merit, with effect from 22nd October, 1939.

### RETIREMENTS

Lieutenant-Colonel J. P. Canteenwalla. Dated 28th February, 1940.

Lieutenant-Colonel M. L. Puri. Dated 13th April, 1940.

Lieutenant-Colonel T. H. Thomas retires on account of ill health. Dated 3rd March, 1940.

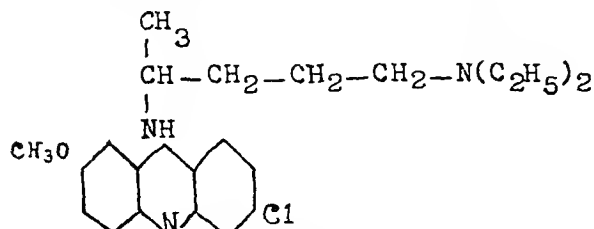
Major G. Dockery retires on account of ill health. Dated 12th February, 1940.

## Notes

### QUINACRINE

#### Composition and properties

QUINACRINE is the dihydrochloride of a synthetic acridine derivative with the following formula:—



2-chloro-7-methoxy-5-diethylamino isopentylamino acridine.

The solubility of Quinacrine in water is about 1 in 100, and the solution gives a neutral reaction. Being a dye substance, its administration may be followed

by a harmless yellow pigmentation of the skin. Where it is desired to administer the drug by injection in cases of coma, in very young children and in cases of gastric upset, Quinacrine Soluble (the dimethane sulphonate of the base) is employed.

Quinacrine acts on the asexual forms of all three malarial parasites, as well as on the gametocytes in benign tertian and quartan malaria, but its action on the schizonts of *Pl. falciparum* is perhaps its outstanding property. Its schizonticidal action seems to be the most powerful of any known anti-malarial remedy.

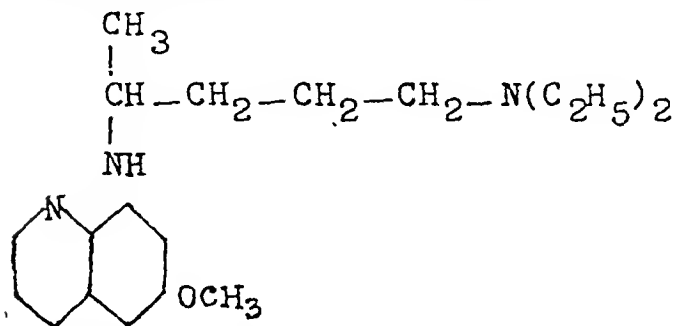
Quinacrine does not cause vertigo, tinnitus or anorexia. Its use is not contra-indicated in pregnancy, in cardiac disease or in blackwater fever. There appears to be some tendency to cumulative effect, and care should therefore be taken to ensure proper spacing of doses and courses of treatment. Quinacrine is of low toxicity, but in susceptible individuals, particularly towards the end of a course of treatment, the drug may give rise to gastric discomfort and occasionally to headaches. These forms of intolerance can be largely prevented by administration of copious fluids and by taking the drug during meals.

Quinacrine Soluble should be given by intramuscular or subcutaneous injection in a daily dosage the same as that of Quinacrine, injections being given once or twice in the course of 24 hours. The contents of the ampoule are dissolved in from 1.5 to 5 c.cm. of sterile distilled water.

### PRAEQUINE

#### *Composition and properties*

PRAEQUINE is a salt of a synthetic quinoline derivative, having the following structural formula:—



8-diethylamino isopentylamino-6-methoxy quinoline.

It is a tasteless pale yellow granular powder relatively insoluble in water but readily soluble in alcohol. It has the power, not possessed by other anti-malarial drugs, of destroying the gametocytes of all types of malarial parasites, and it is therefore of particular value as a prophylactic of the disease. It is usually administered following treatment with Quinacrine in order to diminish the likelihood of relapse.

Praequine is a highly active substance and the prescribed dosage must not be exceeded, otherwise toxic symptoms may appear, e.g., severe epigastric pains, nausea, vomiting, headache cyanosis and methæmoglobinuria. The drug should be used with caution in cases of hepatic dysfunction and of severe anæmia.

A variety of techniques of treatment are in common use. In cases of benign tertian and quartan malaria some authorities are content to give Quinacrine by itself in a course of treatment lasting from six to eight days. The temperature usually returns to normal by the second or third day, and the parasites can no longer be found in the blood stream after the third or fourth day.

Others give 30 grains of quinine in the first two days of treatment and then change over to Quinacrine for the remainder of the eight days' course of treatment.

It is the practice in some localities to follow a six days' course of quinine, after an interval of two days, by the administration of Praequine for a further five days.

In malignant tertian malaria it is common practice to give a six days' course of Quinacrine followed, after a rest period of two days, by a five days' course of Praequine. Praequine is of particular value in this form of malaria on account of its action upon the crescents.

Treatment with Quinacrine given orally may be replaced by twice daily injections of Quinacrine Soluble, in urgent cases, for two or three days after which the drug can be given by mouth.

We understand that a copy of the Quinacrine/Praequine booklet will be forwarded to any member of the medical profession on request to Messrs. May and Baker (India), Limited, 11, Clive Street, Calcutta, India.

### BOVRIL, LIMITED

#### (FORTY-THIRD ANNUAL GENERAL MEETING)

IN 1939 the Bovril sales showed a considerable increase over these of 1938. This improvement was to be expected in our home sales, but considering the many abnormal trade conditions throughout the world the increase in our export trade was a very satisfactory feature of our business.

Since the beginning of the war much of our production has been for the Services, and although demands were often made at very short notice we were able in every case to satisfy them. In this connection it should be noted that our Government contracts are now accepted on a cost basis, and the allowed margin of profit is very small. The Ministry of Supply are to be complimented on this policy, as it enables them to purchase at the lowest possible prices. The manufacturer, however, who is working for the Government on a cost basis may in certain circumstances be involved in losses; this is particularly liable to happen in a business such as ours, where large stocks of raw materials must be held for normal trading. It may be necessary to draw upon these stocks for special contracts; in this case the stocks must be replaced, but often at greatly increased prices. It is, therefore, clear that in these cases the cost should in a measure be based upon replacement prices, otherwise serious losses may be incurred.

In these days of food rationing and long hours of overtime on the part of industrial workers, the need for Bovril and the goodwill towards it is greater than ever. Needless to say, this ever-increasing goodwill is something we intend to foster and maintain.

Like most firms we already find ourselves working short-handed; of the office staff alone 46 members have joined up.

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## Original Articles

### OBSERVATIONS ON SOME UNUSUAL TOXIC EFFECTS OF SULPHANILAMIDE THERAPY

By M. N. DE, M.B. (Cal.), M.R.C.P. (Lond.)

*Professor of Medicine, Medical College, Calcutta*  
and

N. R. KONAR, M.B.

*House Physician, Medical College Hospitals, Calcutta*  
(From the Department of Medicine, Medical College, Calcutta)

SINCE the discovery of prontosil rubrum by Domagk, a large volume of literature has been published recording the results obtained both in the laboratory, as well as clinically, with drugs belonging or related to sulphanilamides. As the latter are being used more extensively and in bigger doses the dangers which may be associated with their administration are more and more appreciated and any further observation on the subject should be welcome.

Amongst the toxic symptoms observed since the early days of prontosil therapy cyanosis is by far the commonest. It is not associated with any respiratory distress and investigations have shown that it is not necessarily accompanied in all cases by a change in the blood pigment. It seems more likely that it is due to the formation of a pigment in the body from the condensation products of the drug itself (Marshall and Walzl, 1937). Posner and his colleagues (1938) described a highly unstable form of methæmoglobin which they thought, might account for cyanosis in some of these cases. In many instances, however, the cyanosis is associated with sulph- or methæmoglobinæmia (both intracorpuseular). Sulphæmoglobinæmia is due to the union of the intestinal sulphuretted hydrogen with hæmoglobin, a reaction which is catalysed by sulphanilamides. This untoward effect may be avoided by withholding purgatives, except very mild ones like liquid paraffin, by giving a low residue diet and excluding articles containing sulphur, eggs, onions, garlic, etc. [Archer and Discombe (1937), Paton and Eaton (1937)]. Methæmoglobin however causes no trouble as it is rapidly reconverted into hæmoglobin when treatment with sulphanilamide drugs is stopped and glucose and oxygen administered.

Nausea with epigastric pain and occasionally vomiting may be produced by this group of drugs. These symptoms are more common with the newer remedy, M. & B. 693. It usually stops after the drug is withdrawn. Drug fever may occur seven to twelve days after the treatment has been started but is not common. A rash occurs in about six per cent of cases [Hageman and Blake (1938)]. Hallam (1939)

reported severe skin rash and general reaction following the administration of M. & B. 693 in a patient who also had exposure to ultra-violet light. He thinks that when the skin is photosensitized by some chemical reaction, following the administration of M. & B. 693, an exposure to moderate doses of ultra-violet light precipitates the onset of intense reaction. Bettley and Simon (1939) reported a bullous eruption due to the use of sulphanilamide. They discussed the various causes of the rash and according to Tedder (1939) put them in three groups: (1) Eruptions due to sensitization. These are somewhat like allergic reactions and can be reproduced even by the administration of a single dose of the drug. (2) Eruptions due to toxic effect of the drugs. These disappear if the dosage of the drug is reduced. (3) Eruptions due to the combined effects of sulphanilamide and light. In the first two groups the rash is more or less generalized but in the third it occurs mainly or wholly on the surfaces exposed to light. Thompson (1939) reports cases of rash resembling measles, rubella and scarlet fever after the administration of M. & B. 693. Agranulocytosis is by far the most dangerous condition produced by these drugs. Fatal granulocytopenia following administration of the sulphanilamide group of drugs has been reported by Sheket and Price (1939), with post-mortem studies. The fundamental picture is that of toxic granulocytopenia with arrest of the development and maturation of the myeloid cells. The authors consider that in these cases quantity and prolonged use of the drugs are more important factors than idiosyncrasy. Although this effect of the sulphanilamide group of drugs on the leucopoietic function of the bone marrow is a serious one and is often discussed, it is not so frequent as may be thought. The writers have not yet seen an instance of this complication during their routine use of M. & B. 693 in the wards of the Medical College Hospital.

Amongst the nervous symptoms which may arise, depression, headache and dizziness are common. Palpitation, paræsthesia, tinnitus and peripheral neuritis have also been noted very rarely.

During the routine use of M. & B. 693 especially in the treatment of pneumonia we often see a condition which may very well be considered as a toxic manifestation and which sometimes gives rise to a good deal of alarm. We have not so far been able to find any reference to this subject. In a case of acute lobar pneumonia, no sooner is M. & B. 693 exhibited in adequate doses, than the patient begins to perspire profusely and the temperature drops down to normal or even subnormal. This condition usually develops 24 to 48 hours after the treatment has been started. In some cases, the sweating is so severe that the patient's clothes have to be changed several times in the

day and night. In such a condition, the skin feels cold and clammy, urine diminishes considerably, the patient looks weak and exhausted and the whole picture resembles that of collapse. This upsets not only the patient's relatives but also the practitioner who is treating the case. Such a dangerous depression of the vasomotor system not only leads to a marked concentration of the circulating toxins but also lowers the temperature of the body and maintains it at a low level. This prevents the development of a healthy reaction of the tissues to the invading micro-organisms and their toxin, and delays the mobilization of an adequate amount of antibodies. Thus actual resolution is often hampered and convalescence chequered by complications with irregular pyrexia.

Hæmolytic anæmia is another rare complication of sulphanilamide therapy. Unlike agranulocytosis it occurs in the first few days of the treatment (usually 2 to 4 days). There is a sudden fall in the number of red cells with varying amount of jaundice and hæmaturia. According to Buttle (1939), no fatal case has yet been recorded.

Though cyanosis alone is the commonest feature of the toxic effect of the drug, profound blood destruction, producing hæmolytic anæmia and death, has seldom been found associated with the cyanosis. In view of the extreme rarity of such a complication compared with the widespread use of the drug, we consider it imperative to report two fatal cases in which cyanosis associated with marked blood destruction developed after the administration of sulphanilamide preparations.

It may be mentioned that one of our patients developed a generalized erythematous rash after taking a drug of the sulphanilamide group for high continued fever after childbirth. But as such eruptions are somewhat common and have already been reported by others, we do not propose to discuss the subject in our present paper.

### Clinical notes

*Case 1.*—R. J. P., aged 43, Parsi male, was admitted under one of the writers (M. N. D.) on 3rd February, 1939, for continuous fever for 12 days. The patient had been a chronic sufferer from antrum disease. The latter was painful recently when he felt feverish (21st January, 1939). The patient had an exposure to short-wave diathermy over the painful area on 27th January after which he had a high rise of temperature with rigor. The fever used to vary between 102° and 105°F. Pulse rate was between 110 and 120 and respiration 32 and 40 per minute. No abnormality was detected in the heart or lungs. Abdomen was distended and tympanitic. Liver and spleen were not palpable. As the temperature was persisting at a high level, the attending physician administered drugs of the sulphanilamide group. The patient had one tablet of prontosil album three times a day for five days from 28th January to 1st February. He had also intramuscular injections of 10 c.cm. of 2.5 per cent solution of prontosil rubrum daily for three consecutive days from 30th January to 1st February. The prontosil was then discontinued as it had no effect on the temperature. He had a plain diuretic and diaphoretic mixture. The patient was kept on liquid diet and his bowels were

moved by soap and water enema. There was no sign of improvement; on the contrary the patient became more and more toxic and developed hiccough on 2nd February. He looked distinctly cyanosed on 3rd February when he was removed to the hospital. On admission the patient was found to be toxic, comatose and markedly cyanosed. The temperature was 105°F. and pulse, which was 126 per minute, was soft and feeble. Blood pressure 110/70 mm. of mercury. Respiratory rate was 36 per minute. Tongue coated, dry and deeply cyanosed. Abdomen distended and tympanitic. Liver and spleen were not enlarged. Heart sounds were feeble and lungs were clear. The tongue, tip of the nose, the lobules of the ear, and the finger nails were bluish in colour. Fifteen ounces of red coloured urine were drawn out with a catheter. He was having frequent, loose, foul-smelling stools.

*Laboratory reports.*—Hæmoglobin—46 per cent, red cells—2,400,000 per c.mm., leucocytes—62,000 per c.mm., polymorphonuclear cells—61 per cent, lymphocytes—26 per cent, monocytes—5 per cent, eosinophiles—8 per cent, malarial parasites—nil, poikilocytosis, anisocytosis, many nucleated red cells and myelocytes present. Examination of the blood 24 hours later showed hæmoglobin—40 per cent, red cells—2,400,000 per c.mm., leucocytes—15,912 per c.mm., polymorphonuclear cells—88 per cent, lymphocytes—5 per cent, monocytes—7 per cent, eosinophiles—nil, malarial parasites—nil, normoblasts, poikilocytosis and anisocytosis present. Halometric index—4.8, size of red cells—7.17 $\mu$ , blood culture—positive to *B. typhosus*, Widal reaction—T, 'H' positive up to 1/125, blood hæmolyzed easily. Spectroscopically it showed bands, characteristic of oxyhæmoglobin. Blood taken for van den Bergh test and bilirubin content hæmolyzed on two occasions.

*Urine.*—Colour—brownish-red, reaction—acid, albumin—present, sugar, acetone, bile salts and bile pigments—nil. Occult blood test—positive. Microscopical examination—a few hyaline casts.

The patient gradually became more comatose and the cyanosis deepened. The respiratory rate went up to 44 per minute and pulse rate to 130 per minute. The temperature was maintained at 105°F. The patient died on 5th February, two days after admission into the hospital.

*Case 2.*—B. C. K., aged 22 years, male, was admitted on the 21st July, 1939, with complaints of swelling of the left inguinal glands for six days and high fever for three days. The patient, who came recently from Assam, had a rise of temperature up to 105°F. associated with swelling of the left inguinal glands and accompanied by headache, vomiting and rigor on the 19th July, 1939, at 5 p.m. An examination of the blood showed a leucocytosis of 10,750 per c.mm. with 78 per cent polymorphonuclear cells. No malarial parasites could be found. The patient took a tablet of prontosil rubrum at 6 p.m. and another at 10 p.m. on 20th July. Throughout the whole day and night, the temperature varied between 103° and 105°F. He was brought to the hospital next morning (21st July). His bowels were constipated. The patient had no quinine, atabrin nor purgatives.

*Condition on admission.*—Patient was semi-conscious and at times delirious. He was jaundiced and markedly cyanosed. Neck was slightly stiff. Kernig's sign positive. Pupils equal and reacted well to light. Eyes congested. There was a generalized flush all over the body. Deep reflexes sluggish. Tongue coated and dry. Abdomen soft. Liver and spleen not palpable. Heart sounds weak; pulse rate 120 per minute. Blood pressure 120 mm. of mercury. Temperature 104°F. Respiration 28 per minute. Lungs clear. Left inguinal glands swollen and tender. Penis, scrotum and testis healthy. On lumbar puncture 25 c.cm. of clear cerebrospinal fluid was drawn under moderately increased pressure. As there was retention of urine, the patient was relieved by catheterization and red coloured urine was drawn out.

*Laboratory reports.*—Hæmoglobin—80 per cent, red cells—4,200,000 per c.mm., leucocytes—15,600 per c.mm., polymorphonuclear cells—78 per cent, lymphocytes—20 per cent, monocytes—2 per cent, eosinophiles—nil,

malarial parasites—none seen, microfilaria—none found, coagulation time—6 minutes, bleeding time—4 minutes, halometric index—1.7, size of red cells—7.32  $\mu$ , platelet count—100,000 per c.mm., reticulocyte—2.2 per cent, partial hæmolytic commencing from 0.5 per cent saline and complete at 0.36 per cent. Blood urea—80 mgm. per 100 c.cm., non-protein nitrogen—64 mgm., cholesterol—130 mgm. per 100 c.cm., van den Bergh reaction and bilirubin content could not be done as the blood hæmolyzed. Spectroscopic examination—presence of methæmoglobin, agglutination reaction—negative to T. A. B. and leptospira, blood culture—no growth. The hæmoglobin per cent came down to 60 within the course of the next 24 hours.

Urine.—Colour—deep red, reaction—acid, specific gravity—1015, sediment—present, albumin—copious. Sugar, acetone, diacetic acid—nil, bile salts and pigments present, indican—nil, occult blood test—positive. Microscopical examination—a few pus cells, red blood corpuscles and epithelial cells. No casts seen. Spectroscopic examination of urine—presence of methæmoglobin.

Cerebrospinal fluid—clear, no white blood corpuscles seen in the centrifugalized deposits. Red blood corpuscles—a few seen in the centrifugalized deposit. Culture—no growth.

Progress of the case.—Patient gradually became more unconscious. His temperature remained high. Bladder had to be relieved by catheter and the bowels by enema. Later on he developed œdema of the lungs and died on the 26th July, the fourth day after admission into the hospital.

### Comments

It will be seen that in the first case, which was a severe attack of typhoid fever, prontosil was administered in moderate doses under a mistaken diagnosis of antrum trouble. The patient had taken altogether 7.5 gm. of prontosil album tablets and 30 c.cm. of 2.5 per cent solution of prontosil. The cyanosis first appeared on the seventh day after the administration of prontosil album was started, and two days after the drug was discontinued. The patient had not taken any purgative or articles of diet containing sulphur. It is true the patient had an exposure to short-wave diathermy one day prior to the commencement of prontosil therapy but it is very difficult to say if this exposure to diathermy had any relationship with the development of cyanosis. It is quite reasonable to believe that the cyanosis was due to the formation of a dark-coloured oxidation product of the drug itself, the patient being unusually susceptible to sulphanilamide and this susceptibility having been further intensified by a severe infection with *Bacterium typhosum*. Whatever might be the underlying factor responsible for the development of cyanosis, the most interesting point is the rapid hæmolytic of red cells resulting in hæmoglobinuria. In many infective diseases, specially when severe, hæmolytic of red cells may sometimes take place in susceptible individuals, giving rise to hæmoglobinuria and methæmoglobinuria. In the case under discussion the patient did not reveal any evidence of hæmolytic although his red cells had been sensitized by the powerful bacterial toxin till a certain concentration of sulphanilamide or its oxidation product in the blood had initiated the explosion, when rapid hæmolytic took place.

Moreover the hæmolytic of red cells might also help in the production of cyanosis, thus starting a vicious circle. Another interesting point in the case was high leucocytosis with increase in the polymorphonuclear neutrophils, a fact which is an unusual effect of the drug on the function of the bone marrow. One useful lesson which one may profitably learn from the study of the above case is not to indulge in indiscriminate use of sulphanilamide drugs in every case of severe infection, as the latter might serve as the 'last straw' and precipitate catastrophe.

The second case, in which the attending physician suspected streptococcal septicæmia superimposed on filariasis, is an example of extreme drug allergy resulting in the formation of methæmoglobin, rapid blood destruction, methæmoglobinuria and hæmaturia. There was a leucocytosis and the hæmoglobin came down quickly from 80 per cent to 60 per cent within 24 hours. Blood hæmolyzed easily and a spectroscopic examination showed bands characteristic of methæmoglobin. There was also considerable damage to the kidneys as the blood urea was raised to 80 mgm. per cent. Both hæmaturia and methæmoglobinuria were noticed. There must have been a great susceptibility on the part of the patient to sulphanilamide drugs as he developed cyanosis with hæmaturia and methæmoglobinuria after taking only two tablets of prontosil rubrum. These symptoms were noticed within 12 hours of the administration of the drug. Apart from the usual toxic effect of prontosil, viz. cyanosis, blood destruction with hæmoglobinuria is the unusual feature. Here also the severe degree of toxæmia, whatever might have been its origin, must have been the primary factor in producing a suitable soil for the subsequent damaging effect of the specific remedy. The destruction of red cells, however, was not so severe as in the first case.

### Summary

1. A brief résumé of the toxic symptoms after administration of sulphanilamide drugs has been presented.

2. Two fatal cases associated with cyanosis and a hæmolytic condition, hitherto unreported, have been described and the possible causes have been discussed. Hæmaturia and methæmoglobinuria were also noticed in the last case.

3. A note of warning has been sounded against indiscriminate use of the sulphanilamide group of drugs in every pyrexial condition.

It is a pleasure to acknowledge our thanks to Lieut.-Colonel J. C. De, M.R.C.P. (London), I.M.S., Superintendent, Medical College Hospitals, Calcutta, for his permission to publish the case notes. We are also indebted to Professor B. P. Tribedi, Professor of Pathology, Medical College, Calcutta, and Bacteriologist to the Government of Bengal, and Professor P. De, Professor of Physiology, for the various pathological and biochemical reports. Thanks are also due

(Continued at foot of next page)



# TREATMENT OF OPIUM ADDICTION WITH LECITHIN AND GLUCOSE AND ITS EFFECTS ON ABSTINENCE SYMPTOMS

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THE problem of addiction to opium in India has been the subject of considerable attention. This is due to the fact, that this habit is prevalent in certain parts of the country and is responsible for producing considerable impairment of the health and general prosperity of the people. It is for this reason that both preventive and curative measures have been the subject of consideration in various provinces with a view to eradicating the evil.

The authors for many years past have been interested in this problem and have evolved a method of treatment of opium addiction which has given satisfactory results in their hands as well as in those of others. A careful study of the withdrawal symptoms and the biochemical and biophysical changes in the blood was made in a large series of cases of opium addiction in the Carmichael Hospital for Tropical Diseases. All these individuals were males and a careful examination showed that they were not suffering from any other ailment of a serious nature before admission. In all cases the usual dose of opium was continued until the patients had become accustomed to their new surroundings and the hospital discipline. During this period the mentality of the patient with regard to the drug habit was carefully studied. It was made clear to him that in spite of all the treatment that he would receive, he may have to undergo considerable inconvenience and trouble from the symptoms which would follow the withdrawal of

(Continued from previous page)

to Dr. N. H. Oonvala, M.B., to whom the first case belonged.

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the drug, and that his active co-operation was absolutely essential at every stage of the treatment. This took from two to five days. After the patient had got quite used to the new surroundings, the supply of opium was suddenly and completely discontinued with the full knowledge and consent of the patient. The ensuing abstinence symptoms were carefully and systematically observed and noted in each case, and efforts were made to combat them by different means. The blood of each addict was examined three times, firstly on admission, secondly during withdrawal and thirdly after the cure, for N.P.N., blood sugar, water content, lecithin and cholesterol content and blood urea.

## Biochemical and biophysical studies

Observations made by such workers as Sollier (1910), Maguin (1909), Pierce and Plant (1928) have shown that in addiction of long duration, general dehydration of the body takes place owing to excessive perspiration, abnormal salivation and obstinate diarrhoea. These facts strongly suggested to us that such a process of dehydration may have an ultimate effect on the fluid content of the blood. We, therefore, undertook to determine the changes in the physico-chemical properties or in the protein fraction of the blood in the addicts treated by us in the hospital. The present authors (1935, 1937) found that, in most of the cases, the state of addiction was invariably accompanied by an increase in the fluid content of the blood, and were inclined to believe that an excessive secretion on withdrawal will have a reverse effect, leading to an increase in the percentage of serum proteins.

The recent work of Chopra and Roy (1937) on the blood-lipoid changes in opium addicts before, during and after withdrawal, pointed to the probability of a diminution in the water content of the blood on withdrawal, which led Chopra and Ganguly (1939) actually to determine the effect of withdrawal on the blood fluid and also to explain, if possible, the rationale of the treatment of opium addiction with lecithin and glucose. Blood sera from the addicts under treatment were examined for total proteins before, during and after the withdrawal of the drug. In most of the cases it was found that concentration of proteins present in the serum before treatment underwent a definite increase during the withdrawal period and returned gradually almost to the pre-withdrawal value after the addict had undergone the prescribed treatment. The increase in the total protein content during the period of withdrawal, as a general rule, runs parallel to the appearance of withdrawal symptoms. Excessive outflow of water from the body causes one of the most marked withdrawal symptoms that have been observed in almost all the cases studied by us. This apparently points to a disturbance in the fluid equilibrium in general. The effect of treatment may, therefore, be taken to have



restored the fluid equilibrium of the system to its previous level.

Chopra, Mukherjee and Chopra (1935) observed that increase of the euglobulin fraction in the serum of addicts probably meant an ultimate drainage of phosphate from the nerve cells. Lecithin treatment was, therefore, suggested on that basis. In the majority of cases lecithin decreased the intensity of withdrawal symptoms and shortened their duration. But in spite of its administration, the abstinence symptoms were very severe in some of the subjects and in these cases intravenous injections of 25 c.cm. of 25 per cent glucose helped to ameliorate the condition. Although lecithin by itself was unable to cope with the severity of the withdrawal symptoms it doubtless removed the craving for the drug in the majority of cases.

The rôle of glucose, in coping with the abstinence symptoms, can thus be understood. By treatment the ultimate effect seems to be the restoration of the water balance. Therefore, any drug that confers a fluid-retaining power to the blood would be expected to have good effect. Carbohydrates in general and glucose in particular are known to possess this water-retention capacity. Glucose, therefore, in addition to stocking the liver with glycogen, to enable it to cope with the unusual strain on this organ during the process of elimination of morphine, helps the retention of water in the blood and keeps up the blood hydration level to its normal value. From the above considerations we may conclude that lecithin tones up the nerves of addicts by supplying the lipo-phosphates, and glucose helps to restore the disturbed water balance. It is therefore not difficult to see how these two together produce the desired effect in removing the drug craving and alleviating abstinence symptoms in opium addicts.

#### *Treatment of opium addicts with lecithin and glucose*

In view of the above biochemical and biophysical findings it was possible to evolve a method of treatment of opium addiction with lecithin and glucose. Briefly the method is as follows :—

On the evening before the treatment is started, the patient is given a dose of calomel (2 to 3 grains), followed by a saline purgative the next morning. The drug is then suddenly and completely withdrawn and the patient is watched for the development of withdrawal symptoms, which in the majority of cases start on the same day and attain their maximum within 24 hours. The actual treatment was formerly started when the withdrawal symptoms became intense and unbearable, in order to study the biophysical and biochemical changes which are produced in the individual during this period. Lately it has been found distinctly advantageous to start lecithin and glucose the day before opium is withdrawn so that the inconvenience to the patient is reduced to a minimum.

Lecithin (Ovo lecithin, Merck) is given by the mouth in form of pills containing 5 to 20 grains three times a day, and continued usually for five consecutive days. In a number of patients lecithin by mouth causes nausea, and in such cases, the drug may be given in the form of a colloidal solution by injection, the usual dose being 2 c.cm. of 1 per cent solution, twice daily. Experience has shown that lecithin, when given by injection, acts better than when it is given by the mouth. Besides this, the amount required to produce the desired effect is comparatively small and consequently the cost of treatment is considerably reduced. During the period of abstinence the patient is encouraged to take plenty of fluids and glucose by the mouth, as these greatly ameliorate the symptoms of withdrawal.

There is no doubt that in the majority of cases lecithin decreases the intensity of the withdrawal symptoms and shortens their duration. In spite of its administration in some of the patients the abstinence symptoms were severe and in these cases intravenous injections of 20 c.cm. of 25 per cent glucose as well as glucose by the mouth greatly helped to ameliorate the condition. These are given with a view to stocking the liver with glycogen, and in order to enable it to cope with the strain, which no doubt falls on this organ, during the process of elimination of morphine and other alkaloids of opium from the system. We usually give an intravenous injection of glucose every morning for the first three or four days, and if necessary repeat it in the evening when the symptoms are severe. The injections are then stopped and glucose, if still required, is given by the mouth. In severe cases attended with cramps it was found that addition of 10 c.cm. of a 10 per cent solution of calcium gluconate to the glucose solution given intravenously helped greatly in ameliorating this symptom. No other drug is necessary during this period except a brisk saline purgative every morning to help in the elimination of the alkaloid through the gastro-intestinal tract. No further treatment as a rule is required after the first week.

The diet during this period is light because patients, as a rule, cannot take much on account of the gastro-intestinal disturbances produced by the withdrawal. Glucose, milk, and fruit juices are given freely by the mouth for the first two or three days during the withdrawal period. On the fourth day, when the abstinence symptoms begin to disappear and the appetite returns, a diet rich in proteins and lecithin in the form of eggs, milk, beans, fish, chicken, fruits, bread and butter is given.

After the completion of the actual treatment, that is after the complete withdrawal of the drug has been effected, the patients are kept under observation in the hospital for a fortnight or more. A twenty-four hours' specimen of urine is examined for the presence of morphine, in order to see if any of the patients are taking

the drug secretly. In the ordinary course of events the alkaloid can be detected in the urine for four to five days after the withdrawal of opium; after that it cannot be detected except in rare cases where excretion is prolonged. If, therefore, after this period the alkaloid was still found, the presumption was that the patient was taking the drug. If repeated examinations of the urine show the absence of alkaloids it was concluded that the drug was no longer being taken and the habit is cured\*.

On the second day of the actual treatment, most of the patients report that the discomfort had decreased by half. When seen a few weeks after the treatment, many report that the drug had lost its taste and charm and in some cases very small quantities of it produced the sensation of nausea. The treatment undoubtedly

\*For the detection of morphine in the urine the method of Deckert (*Klin. Woch.*, 15, 697, 1937) was followed:

Ten c.cm. of the urine is heated with 0.3 gm. of  $\text{Na}_2\text{CO}_3$  until the first bubbles rise and is then quickly cooled. It is then transferred to a separating funnel and thoroughly shaken with 10 c.cm. of acetic ether. After the layers have separated, the acetic-ether layer is transferred to a small porcelain dish through a filter-paper and evaporated to dryness on a water-bath. The residue is diluted in 0.25 c.cm. of water with one drop of nitric acid (sp. gr. 1.15) and a drop of 10 per cent ammonium molybdate solution added. After careful whirling of the porcelain dish, the contents are filtered through a compressed cotton plug placed in the upper part of the neck of a funnel. The dish is rinsed with two successive quantities of water (0.25 c.cm. and 0.15 c.cm.) which are passed through the filter. The cotton plug is then pressed down to the lower opening of the funnel, so that no filtrate remains in the funnel. A drop of 2 per cent solution of ammonium vanadate is then added and well mixed. A turbidity develops, depending on the morphine content.

gave rise in a number of cases to a definite feeling of aversion for the drug, whether by smoking or by the mouth, and the craving for the drug was stopped and cure was effected.

In order to effect a permanent cure a complete overhaul of every patient was carried out with a view to determining if any septic or toxic foci were present in the body, as morbid conditions of this kind are a common cause of opium addiction in this country. If routine laboratory examinations revealed such conditions as dysentery, sprue, helminthiasis, sinusitis, conjunctivitis, etc., these were treated during the period of observation after treatment.

The mental outlook of the addict also showed a remarkable change. After the treatment the persons who were sad, morose, apathetic and who had pale and sallow complexion, became cheerful, ate well, improved in general health and put on weight. They became more sociable, docile and respectful and showed inclination to do their ordinary work. They now felt interested in their surroundings and were observed to be more active than other patients in the hospital. After discharge from the hospital, it was ascertained that most of them had become useful members of society and followed their vocations with interest.

#### *Abstinence symptoms*

We will now briefly describe some of the chief abstinence symptoms met with in the patients treated in this series and how these were controlled.

#### *Nervous and psychical disturbances*

A perusal of table I will show the nature, frequency and course of the common nervous disturbances, which were encountered in this

TABLE I

*The nervous and psychical disturbances in a series of 200 opium addicts on sudden withdrawal of the drug*

Symptoms	Frequency, per cent	Time of onset	Time of maximum intensity	Time when they disappeared	Remarks and symptomatic treatment if necessary
1. Yawning, lassitude, general depression and restlessness.	95	1st day	3rd and 4th day.	4th day	Mixture containing iron and strychnine is helpful if they persist after 4th day.
2. Cramps and pains in limbs.	80	2nd "	3rd day	5th "	Calcium gluconate intravenously, massage, glucose by mouth, aspirin, barbiturates.
3. Headache ..	50	3rd "	4th "	7th "	Aspirin and barbiturates are helpful.
4. Paræsthesias ..	15	3rd "	5th "	7th "	Bromides, valerian and calcium are helpful.
5. Tremors of hands ..	6	3rd "	5th "	7th "	No special treatment required.
6. Emotional disturbances, feeling of impending death, melancholia.	15	3rd "	5th "	10th "	Occupational therapy.
7. Insomnia and nervous excitability.	80	1st "	3rd to 5th day.	10th day after.	A very troublesome symptom, yields to hot foot bath before retiring, massage, barbiturates, liquid extract of <i>Rauwolfia serpentina</i> in 10 to 15 minim doses every night.

series after complete and sudden withdrawal of the drug.

#### *Digestive disturbances*

The effects on the alimentary system are severe when the patient is taking the drug in large doses. The results of analysis of various symptoms pointing to the derangement of the digestive organs have been summarized in table II.

showed any remarkable abnormality except in one case in which signs and symptoms of serious heart block were observed on withdrawal of the drug. This gradually disappeared after a week and no special treatment was necessary except the usual administration of glucose intravenously.

The total course of treatment varied from 7 to 12 days and during this period the change in the condition of the addicts was remarkable.

TABLE II

*The digestive disturbances produced in a series of 200 opium addicts on sudden withdrawal of the drug*

Symptoms	Frequency, per cent	Time of onset	Time of maximum intensity	Time when they disappeared	Remarks and symptomatic treatment if necessary
1. Anorexia and distaste for food.	80	2nd day	4th to 5th day.	8th to 10th day.	No special treatment necessary.
2. Epigastric pain and abdominal disturbances.	28	3rd "	4th to 6th day.	8th day	No special treatment necessary and if they persist after 8th day may be due to intercurrent diseases such as hookworm, or chronic bowel infection, etc., which should be properly diagnosed and treated.
3. Diarrhoea ..	45	2nd "	3rd day	5th "	No special treatment necessary.
4. Nausea and vomiting	38	2nd "	3rd "	6th "	Ice to suck and 10 drops of adrenaline hydrochloride (1 in 1,000) sublingually.
5. General abdominal discomfort and pain.	18	4th "	6th "	14th "	Keep bowels open with purgatives. Lavage of the stomach.

#### *Disturbances of body secretions*

General imbalance of secretions of the body is a very common phenomenon after withdrawal of opium. The symptoms observed under this heading have been tabulated in table III.

The patients treated in the hospital were kept under further observation for a period varying from 4 to 12 weeks in order to rehabilitate and train them to the new environment, and to watch for any relapse occurring. The

TABLE III

*The imbalance of general secretions of the body as seen after withdrawal of the drug in 200 opium addicts*

Symptoms	Frequency, per cent	Time of onset	Time of maximum intensity	Time when they disappeared	Remarks and symptomatic treatment if necessary
1. Running of the nose and sneezing.	70	1st day	3rd day	5th day	If these persist after the 5th day, an examination of the nasal cavities and accessory sinuses may reveal some pathological condition, which may be radically treated by operation or by general treatment.
2. Lacrymation ..	55	Few hours	2nd "	4th "	If these persist then treat the cause, <i>i.e.</i> , blepharitis, trachoma, opacities, etc.
3. Salivation ..	20	1st day	3rd "	6th "	No treatment necessary.
4. Sweating ..	10	2nd "	3rd "	7th "	Do.
5. Spermatorrhœa ..	5	4th "	6th "	7th "	Bromides.

#### *Cardio-vascular system*

Electrocardiographic examinations of patients were made before withdrawal, during withdrawal and after treatment. None of them

period of rehabilitation and rebuilding of the personality of an addict may sometimes extend to a few months, according to the personality of the addict.

### Results of the treatment

The results obtained in the special hospital series are given in table IV.

Table IV shows that complete cure was effected in 70 per cent of this series. The dose was reduced by 80 per cent in 10 per cent, and by 50 per cent in 15 per cent of cases. The treatment failed completely in 5 per cent of the series, and there was a relapse to the habit in the remaining 5 per cent. Thus it appears that the results are more encouraging (i.e., 70 per cent cure) than with any other forms of treatment which have so far been tried in this country.

It may be of interest to state that in April last the senior author was requested by the Government of Assam to help and advise them in connection with the opium prohibition campaign which was being started there and he deputed the junior author to go and work in the field. Before actually starting the campaign a large number of medical men were trained in the method of treatment with lecithin and glucose and over one hundred treatment centres were established in the Upper Assam Valley, where prohibition was to be started. During this campaign nearly 12,568 addicts were successfully treated.

### Summary and conclusion

On the basis of the biochemical and biophysical investigation into the blood of opium addicts it has been possible to evolve a new method of

### RADIOLOGICAL APPEARANCES OF THE HEART AND LUNGS IN CASES OF HYPERTENSIVE HEART FAILURE\*

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A FLUOROSCOPIC examination of the chest is frequently rewarded by valuable information, in cases of high blood pressure. It was with a view to gaining further insight into the radiological problems associated with hypertensive heart failure that the present investigation was undertaken.

A large number of cases of high blood pressure with signs of cardiac failure have been examined fluoroscopically, in order to determine radiological appearances, characteristic of this type of case. In order to determine the exact shape of the heart and the cardiac measurements, thirty-five cases of hypertensive heart failure were subjected to orthodiagraphy; in some of these cases, teloradiograms were also taken. Investigations were limited to subjects

\* Working with the aid of a medical research grant from the trustees of the late Sir Ratan Tata.

12,000 addicts, with very good results. The cost of the treatment is reasonable.

TABLE IV

Results of treatment in a series of 200 opium addicts

Results	Complete cure effected	DOSE REDUCED		Complete failure	Relapse within six months after discharge from the hospital
		80 per cent	50 per cent		
Cases treated in special series 200 ..	140	20	30	10	10
Percentage .. .. .	70	10	15	5	5

treatment of opium addiction. Its effects upon different withdrawal symptoms have been discussed. It would appear that the central nervous system and the digestive system bear the brunt of this addiction and the symptoms produced during the abstinence period are greatly modified and ameliorated by this treatment. The course of treatment varies from 7 to 12 days. The results of the treatment are very encouraging and better than other forms of treatment tried by us. This treatment is suited for mass treatment and has been successfully used in a campaign in Assam in a series of over

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ranging in age from forty to seventy; the systolic pressure in no case was under 160 mm. of mercury, while one or more signs of cardiac failure, either 'left-sided' or 'right-sided' or both, were present in all cases selected for detailed investigation.

The impressions gained from this clinical material have been incorporated in the present paper; a much larger series of cases must be investigated before assuming the following deductions as representative of hypertensive heart disease, in general.

#### *Radiological appearances*

For the sake of simplicity, the radiological appearances of the heart, aorta and lungs in hypertensive heart failure are considered separately.

*Cardiac silhouette.*—At first sight, there appears to be no constancy about the size or shape of the cardiac silhouette in such cases. Closer inspection, however, permits classification of the silhouettes into certain distinct types. I have come to recognize five main types of cardiac silhouette in these cases:—

(1) In a few of the cases, there is no apparent abnormality of the cardiac silhouette, either in shape or size; the cardiac contours appear normal on inspection; measurement of the various diameters of the heart reveals no abnormality. Such a perfectly normal silhouette is compatible with hypertension of even moderate severity and long standing. One of my male patients, aged 60, has had a systolic blood pressure over 200 mm. of mercury for more than five years, and yet his heart is normal, both clinically and radiologically. A woman of about 50 was observed over a period of six months, at the Liverpool Heart Hospital, with a pressure persistently fixed at 300 mm. of mercury and yet at no time was there any indication of cardiac enlargement, clinically or radiologically.

The degree of enlargement of a heart is no guide to the height of the blood pressure in a given case; for instance, severe grades of cardiac enlargement are not infrequently seen with pressures of 160 or 180 mm.; conversely, cases with pressures well over 200 mm. have shown little or no enlargement of the heart.

A heart that is normal radiologically is not necessarily normal pathologically, for minor degrees of hypertrophy are not detectable even by expert radiologists. According to White (1931) an increase of as much as fifty grammes in the weight of the heart may pass undetected radiologically.

The presence of a normal cardiac silhouette in cases of severe or long-standing hypertension may be explained along the following lines:—

(a) The high blood pressure may be of too short a duration; one should realize that hypertrophy of heart muscle is a slow process taking weeks or months to develop; also, that hypertrophy in the early stages causes no change in the contour of the heart, and hence escapes

detection. This line of reasoning, however, fails to explain the great majority of cases, where the high pressure has existed for more than a few weeks.

(b) If the heart be small to begin with, of the type known as the 'hypoplastic', 'vertical' or 'drop' heart (frequently observed in individuals prone to tuberculosis), then increase in size will not be apparent for some considerable time after the onset of hypertrophy. It may be months or even years before the hypertrophy becomes detectable, radiologically, in such cases.

(c) If the hypertrophy of cardiac musculature, in cases of hypertension, be limited to certain sections of the heart only, then it may remain undetected for some time after its onset. The investigations of Kireh (1930) show that in the early phases of hypertension, hypertrophy of the left ventricle is not diffusely distributed but remains confined for some time to the 'outflow tract' of that chamber (i.e., that region of the left ventricle which extends from the apex to the aortic orifice). Even within the confines of the 'outflow tract' itself, hypertrophy starts first in the terminal portion, that is at the aortic end of the tract rather than at the apex.

Since the region of the 'outflow tract' adjacent to the aortic orifice (i.e., the site of early hypertrophy) does not form part of any border of the cardiac silhouette, lack of demonstrable enlargement of the heart in the early phases of hypertension becomes understandable. The only alteration in the silhouette, in such cases, is in the nature of 'elongation' of the heart, with the apex over-riding the diaphragmatic contour.

Out of a total of thirty-five cases, investigated from the point of view of heart size, five showed perfectly normal cardiac silhouettes.

(2) The 'duck-shaped' or 'boot-shaped' heart (figure 1). This was observed in just over

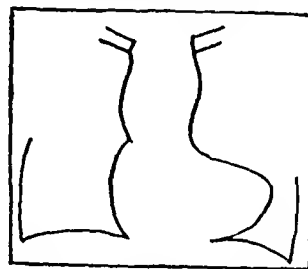


Fig. 1.—'Duck-shaped' or 'boot-shaped' heart.

a third of the cases studied. It represents a local or preponderant hypertrophy of the left ventricle. The main features of such a cardiac silhouette are: (a) A 'rounding of the cardiac apex'; this has been attributed to hypertrophy of the apical portion of the 'outflow tract'. (b) The lower portion of the left border of the heart becomes more rounded or outwardly convex than normal. (c) The most lateral point of the left border of the heart is situated on a much higher plane than normally. (d) The

In nearly-all fever cases, on admission to hospital, blood culture was taken as a routine. Media used were glucose broth and bile salt media. From  $1\frac{1}{2}$  to 2 c.cm. of blood from the patient was added to each of the above media at the bedside and incubated for at least 5 days (in some cases up to 10 days) before declaring them 'negative'.

#### Blood smear examination

(a) Out of 56 cases, a blood smear was examined in 55 for malaria parasites and differential leucocyte count. Only one case showed mixed infection of benign tertian malaria and typhus fever.

(b) Differential leucocyte count:—Polymorphonuclear cells ranged from 60 to 82 per cent. Lymphocytes counted from 16 to 32 per cent. Large mononuclear cells ranged from 1 to 8 per cent (excepting the case with infection of malaria which gave 9 per cent). Eosinophiles counted from 0 to 5 per cent.

#### Weil-Felix reaction and Widal test

Sera of patients were put up for these tests according to history and provisional diagnosis, and repeated if necessary.

#### Technique in brief

Concentrated alcoholized suspensions of OX19, OX2, and OXK for Weil-Felix reaction and dead emulsions of T. 'H', Para A 'H' and Para B 'H' and concentrated alcoholized suspension of T 'O' for Widal tests were used. These suspensions and emulsions were obtained from Kasauli. All sera were tested against OX19 and OX2 as a routine and if both gave negative results combined with negative results in Widal test, the sera were put up against OXK.

Routine dilutions of sera put up in both tests were in 1 in 25, 1 in 50, 1 in 125 and 1 in 250 with controls. In some cases further tests with higher dilutions were also put up.

Dreyer's tubes were kept in a water-bath at 52°C. for 4 hours and then in an incubator at 37°C. for 15 to 20 hours. Readings were then taken by the aid of Dreyer's comparator with lamp. Before decisive readings were taken, sediment at the bottom of each tube was disturbed from the higher to the lower dilutions to distinguish true agglutination from mere sedimentation. To express the results in standard agglutination, Dreyer's reduction tables were used.

A patient whose serum gave standard agglutination of any of the three proteus strains at least in 1 in 125 dilution combined with other findings, clinical and laboratory, has been included in this series of typhus fever, while cases giving positive standard agglutination in lower dilution than 1 in 125 are not included.

The commonest local strain in Bangalore is proteus X19 but a few cases of OX2 are also met with.

#### Result of Weil-Felix reactions

Proteus strain	Number of cases	Percentage positive
OX19 ..	50	89.3
OX2 ..	5	8.9
OXK ..	1	1.8 (imported case)
<b>TOTAL ..</b>	<b>56</b>	<b>100.0</b>

#### Results of Widal tests

Total number of cases tested ..	56
Number of cases negative ..	42

The remaining 14 cases showed agglutination of one or two enteric organisms either in 1 in 50 or lower dilutions.

#### Urine and stool culture

In 17 cases cultures of urine and stools were done and, in each of these, 3 specimens of urine and stools were cultured on 3 consecutive days after the temperature returned to normal. So, 51 urine and 51 stool cultures were done, and all were negative as regards enteric and proteus group of organisms.

#### Wassermann reaction in typhus cases

Stott (1935) cited a case showing a strongly positive Wassermann reaction during the febrile stage, and negative during convalescence and later without any antisyphilitic treatment. The question arises whether a certain percentage of typhus cases like those of malaria do show positive W. R. or not? Sera of 25 definite cases of typhus during the febrile stage were tested for W. R. In 24 cases the reaction was negative but in one case it was positive (W. R. +), becoming negative during convalescence, showing that there is a possibility of a typhus case giving positive W. R., though only during the febrile stage.

#### Symptoms

1. *Temperature*.—Onset is nearly always sudden with headache and rigor. In most cases it is continuous and remittent, but in a few even intermittent.

The following table gives the duration of all the cases:—

Duration in days	Number of cases	Duration in days	Number of cases
8	1	16	6
11	5	17	5
12	5	18	1
13	12	19	1
14	7	27	1*
15	12	* Complicated by pneumonia and recovered.	

In 93 per cent of cases the duration of fever is 11 to 17 days and the extremes are 8 to 19 days.



The fall is usually by lysis and in some cases the temperature takes a week or so to settle down to normal.

#### Other symptoms

**Rash.**—Roseolar rashes appear almost all over the body, mostly over the chest, back, palms, forcarms, and soles. Twelve out of this series (all of whom had fair skin) showed typical rash, but it is always difficult to decide about the rash in dark-skinned persons.

**Bronchial symptoms.**—The respiratory tract is not found to be involved as a rule, as some authorities believe, but bronchial symptoms are fairly common. Twenty-four, i.e., about 43 per cent of the cases, suffered from cough and other bronchial symptoms and signs, and 1 case developed pneumonia but recovered.

#### Diagnosis

All cases were diagnosed on the clinical symptoms and signs along with Weil-Felix reaction. Cases whose sera agglutinated any of the three strains either in a dilution of 1 in 125 or over were diagnosed as typhus fever.

#### Prognosis

It is good; and no death was recorded in this series of cases. Hyperpyrexia, toxæmia, and complications such as broncho-pneumonia were noticed.

#### Treatment

There is no specific treatment for the disease. Symptomatic treatment with good nursing always proved enough to bring about cure.

#### Discussion

It was suggested by Lieut.-Colonel Hance, I.M.S., the residency surgeon, that fever cases, whose sera do not agglutinate *B. typhosus* and *B. paratyphosus* A, and agglutinate *B. paratyphosus* B only, though in a low dilution, along with negative blood cultures, but otherwise running a course like those of enteric fever may be typhus cases. This view was confirmed by subsequent laboratory tests and about 2 cases a month were diagnosed in these two hospitals as 'typhus fever'. Apart from this there are likely to be more victims who did not come to these hospitals and were treated by local medical practitioners.

From the fact that only one case was notified before this work was taken up, and from talks the writer has had with private practitioners in Bangalore during these years, it was stated that the existence of the disease with which most of them are now familiar was not known to them before. It is recommended, therefore, that blood of continuous fever cases should not only be tested for Widal reaction but also simultaneously for Weil-Felix reaction against proteus X19 and X2 as a routine.

The most important factor in the diagnosis of typhus fever is the Weil-Felix reaction. It is found that some sera from non-typhus fever

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## COMMON COLD RESPONSIBLE FOR GRAVE SUSPICION OF RABIES IN THE DOG AND A DISCUSSION ON ASSOCIATED CONSIDERATIONS INCLUDING RABIES IN MONGOOSES AND BATS

By S. D. S. GREVAL

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THE intention is (I) to describe observed cases and give crucial points in the differential

(Continued from previous column)

cases do agglutinate proteus strains in low dilutions, but never higher than 1 in 100. So, it is safe to diagnose a continuous fever case as typhus whose serum has agglutinated any of the strains in 1 in 125 dilution or higher. In doubtful cases Weil-Felix reaction should be repeated after a few days to find any rise in titre.

#### Summary

1. Fifty-six cases of typhus fever were diagnosed and treated in the Bowring and Lady Curzon Hospitals, Bangalore, during 1936, 1937 and 1938.

2. Incidence.

(i) All ages above 8 years, mostly adults, have suffered.

(ii) Both sexes, mostly males, were the victims.

(iii) The disease prevails in all communities, but mostly among the poor.

3. In Bangalore typhus is more prevalent (i) during spring and autumn and (ii) in the thickly populated areas.

4. The nature of vector of disease in Bangalore is still to be investigated.

#### Acknowledgments

My thanks are due to Lieut.-Colonel J. B. Hance, I.M.S., for valuable suggestions and permission to publish this article. It is my pleasant duty to acknowledge the help and co-operation rendered by the staffs of the pathology department and the Bowring and Lady Curzon hospitals, particularly to Dr. A. St. C. Bartley, Dr. M. R. Sirsi and Dr. Ramchandra Rao.

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diagnosis of rabies, (II) to recommend a line of prophylaxis for humans who have been bitten or have come into contact with the saliva of a suspicious dog of the kind described, (III) to comment on isolation *versus* destruction of the dog and (IV) to add a note on mongooses and bats as carriers of rabies.

### I. Observed cases

(i) *A case recently observed.*—A male dachshund, aged 4 years, belonging to one of the writers (S. D. S. G.) was observed on 19th March, 1940, to have congested eyes. The right eye was kept partly closed. Minor injury was suspected and eye drops (zinc sulphate 0.25 per cent) instilled. In holding the dog for the drops it was observed that the nose was full of mucus which was discharged by sneezing immediately after the drops. This occurred in the evening and the dog retired as usual to his basket on the verandah on the ground floor. He was quieter than usual during the night.

Next morning, he showed signs of malaise and weakness. Nose was hot and dry. Stairs were negotiated deliberately instead of with a bounding rush and a position in the sun on the top verandah (usual in winter) sought. Warm milk with sugar was given. Condition appeared to improve. The usual daily food (bones with meat and *chapati*) was refused. Evening stroll was not allowed.

On 21st no change for the worse was observed. The weakness had disappeared.

On 22nd milk and sugar diet was given during the day and fried liver (a weekly ration) at night. No stroll was allowed. The dog was observed to pass large quantities of water standing on all fours like a puppy, in the compound.

On 23rd at midday it was observed that the dog could not close its mouth and that after drinking water the last lap of water flowed out of the mouth together with frothy saliva. He was isolated on the top verandah and on being left alone showed unusual restlessness. By 4-30 the mouth was open, copious froth appeared with attempt at drinking water and ropy saliva was hanging from the angles of the mouth at rest. The second writer saw the dog at this stage. Provisional diagnosis of rabies was made and the dog secured, by a strong double rope tied to the verandah railing, for further observation.

Points for the diagnosis were: (i) dropping of the jaw, (ii) foaming at the mouth and thick ropy saliva, and (iii) a slight restlessness.

Points vitiating the value of the above points were: (i) although the jaw was dropped, the tongue was normal in colour and action, (ii) foaming at the mouth occurred only with drinking water, (iii) the restlessness was not marked and was due to confinement, (iv) sleep was normal, and (v) bark and growl were normal.

Points definitely against the diagnosis of rabies were: (i) no alteration in the familiar gaze, (ii) no movements indicative of muscular inco-ordination, (iii) no ferocity, and (iv) no weakness anywhere excepting the lower jaw. Importance of individual peculiarities of movements must here be mentioned. The dog always lifted a leg when moving fast and dragged his hind quarters when moving a few inches (suggestive of dumb rabies in a sick dog seen for the first time).

History of a dog bite was negative; of a probable mongoose bite, diagnosed from the shape of the bite and the presence of a wild mongoose in the locality over a year ago, positive; and of a bat bite a few days previously possible on account of an angular bleeding scratch (likely explanation, however, being ends of wires in the garden). Both wild mongooses and bats are seen very close to the house.

The second writer at this stage remarked that his dog had shown the same symptoms last year, about the same time, for two days.

No stool or urine was passed this day. Lightly fried liver cut into small pieces was greedily devoured. Two

pieces bigger than the rest were ejected with a short cough but ultimately chewed with great exertion and swallowed. On the ejected pieces curdled milk was seen. Evidently there was a stasis of food in the pharynx.

A short stroll was arranged, and the dog passed urine. On 24th morning the condition was unaltered. The question of commencing prophylactic treatment for the family and the servants was considered.

By evening the condition was improving. Although foaming at the mouth appeared with drinking, there was no flow of saliva otherwise. The mouth was not open to the same extent. The idea of commencing the prophylactic treatment was shelved. The dog was taken out for a stroll. Stools and urine were passed. Diet of milk and liver was continued.

On 25th morning the condition was found to have improved further. There was no foaming when the dog drank water. The process, however, was very slow and the water was made opalescent and tinged salmon-pink. Even big pieces of fried liver were greedily devoured.

During the day a tailor remarked that he had recently seen at Shamnagar near Barrackpore, dogs which were foaming at the mouth like mad dogs but not biting anyone. It was now decided to call in a veterinary surgeon to obtain information on the prevailing diseases.

In the evening a veterinary practitioner of experience was called. He stated that the condition was due to a chill. He had treated a few days previously two newly-imported dogs suffering from the same condition. The pathology of the condition was inflammation of the sub-maxillary glands which interfered with the elevation of the jaw. When asked to confirm by palpation he did so. No external swelling, however, was visible and the dog did not give any indication of pain when the palpation was done. Salicylates or tincture of iodine internally was recommended. In the opinion of the veterinary practitioner the evidence was 99 per cent against rabies.

On 26th the condition was found to have improved still further. Difficulty in drinking water still persisted. The water was still rendered opalescent and tinged pink. The deposit from the water gave the chemical test for blood and consisted of granular debris, epithelial cells, and an abundance of mixed flora.

Tincture of iodine (B. P.) 2 minims inside a butter bolus was given.

All semi-solid and even solid food was readily swallowed. Milk was refused and water preferred.

On 27th improvement continued. The dog in spite of at least 8 days' illness appeared neither weak nor thin. The diagnosis of rabies was given up.

On 28th the dog was discharged from isolation.

All usual habits were quickly resumed.

### (ii) Previously observed cases recalled.—

Three other cases have been included in the foregoing description. They are one Calcutta-bred wire-haired terrier belonging to the second writer and two imported great danes seen and treated by the veterinary practitioner. Then there were the dogs observed by the tailor at Shamnagar near Barrackpore Bazaar and village information in rabies is not unreliable. The ownerless dogs are not without keepers altogether. They are many peoples' common pets and a marked change in them is bound to be noticed by someone. This is especially true of the village dogs.

### II. A line of prophylaxis for humans who have come into contact with suspicious dogs of the kind described

The prophylaxis planned in the present case represents the writers' recommendation. Three

subjects were considered for antirabies treatment: (i) the first writer who had a ruptured blister on the sole of one foot and might have trodden bare-footed on a spot of saliva on the floor of his bedroom on 23rd March before the dog was isolated; (ii) his son under 3 years of age who in the garden threw a handkerchief into a collection of water from which the dog had drunk, picked it up and then dropping it under harshly given instructions put his fingers in his mouth in embarrassment (entry of dog's saliva into the mouth); and (iii) a servant who was particularly friendly with the dog. None of these subjects were bitten. The third subject had neither blisters nor swallowed the dog's saliva yet his close association with the dog made it possible for the saliva to come into contact with a not readily visible breach in his skin. The first writer has reported a death from rabies in a victim to whom prophylactic treatment was not given because no visible breaches in his skin had been found, and cited other instances (Greval, 1936). A death is occasionally reported even in treated cases of class I (licks only). Two such deaths appear in the Annual Reports of the Pasteur Institute of India, Kasauli, for the last two years (Smith, 1938; Webster, 1939). A statistically-inclined reviewer, opposed to giving treatment when the skin is unbroken (no obvious bite or wound, S. D. S. G.), called the writer's case 'unfortunate' (McKendrick, 1936). The League of Nations Report on Rabies (Marie *et al.*, 1927) leaves open the question of treating licks. A textbook on medicine with a section on rabies written by a medical man with Indian experience definitely discredits treatment as superfluous for licks without obvious bites or wounds. With such views and advice the writers' opinion is definitely at variance. They hold that the infection depends more upon the infectivity of the rabid animal than upon the severity of the bite or the susceptibility of the bitten animal. That is why the infection rate in different batches of bitten humans and animals varies from *nil* to 80 or 90 per cent (Harvey and McKendrick, 1923). A capricious variation in the infectivity alone is much more likely than in both the severity and the susceptibility. The well-known fact that every strain of street virus, proved to be so clinically and microscopically, does not succeed in passage, strengthens this hypothesis. This statement has been repeated from a previous publication (Greval, 1936) in view of the difference in opinion and of the risk run by those who are refused treatment. Cases of licks by definitely rabid animals *must* be treated as cases of medium severity at least.

Had the dog got progressively worse, weakened and died of the disease he was suffering from in a few days, and the brain been examined for Negri bodies and found negative, should the three subjects at risk have been given treatment? In the writers' opinion, yes. A negative microscopical finding should not interfere

with clinical finding or presumption, when the result would be fatal. Development of the Negri body is a gradual process and the dog may die before it is developed.

Could the dog have had an abortive attack of rabies from which he has recovered but which made him infective? Such a possibility cannot be ignored. It has been known since Pasteur's time (Marie *et al.*, 1927). The points against the diagnosis of abortive rabies are: (i) there was no mental change or neuro-muscular weakness, apart from the one suggested by the open mouth, and (ii) three other dogs suffered from similar symptoms and recovered (recovery from rabies is an extremely rare event).

The possibility of recovery from rabies and the consequent latency of infectivity was perhaps given more importance than it deserves by the International Rabies Conference of 1927 when it recorded 'Hitherto doctors, veterinary surgeons and laymen have been unanimous in asserting that there is no danger of rabies if the biting animal is still alive. This view is entirely erroneous . . .' (Marie *et al.*, 1927). In Indian experience the well-known rule that there is no risk to the contacts if the dog is alive and well for 10 days after the contact, followed at all the Pasteur institutes and antirabies centres in India, has worked very well (Shortt, 1933). The first writer remembers a dog which died on the 11th day of observation and was proved to be rabid microscopically. It was not, however, well on the 10th day (*alive and well* should go together).

Reports have been received of deaths from hydrophobia in subjects bitten by dogs which were healthy when the subjects died. The culpability of such dogs, however, has remained not proven. The following account is quoted from the last Annual Report of the Pasteur Institute of India, Kasauli (Webster, 1939).

'An interesting case of hydrophobia was reported from Faridkot centre. A man developed hydrophobia two months after being bitten by a dog which was quite healthy when the patient developed the disease and died. On an enquiry being made from the Chief Medical Officer, Faridkot State, as to whether there was another possible source of infection he writes:—

"Although there is no definite history of his having been bitten by any other dog but this cannot be excluded."

### III. Isolation versus Destruction

Authorities frequently issue orders which make it appear that securing and destroying a dog supposed to be rabid are of the same value. This definitely is not the case. By destroying a suspected animal, *before* the Negri body has developed, the suspicion may never lead to a positive microscopical finding of rabies. The negative microscopical finding will lead to (i) many medical advisers not recommending treatment, (ii) many cases at risk not taking

treatment, and (iii) many cases taking treatment half-heartedly. The opposite danger also exists. A dog like the ones described and cited may be regarded as rabid and killed, and quite a large number of people given treatment needlessly. Apart from inconvenience, expense and waste of time, the treatment is not altogether devoid of sequelæ.

Securing a dog, particularly a pet dog which is not already suffering from furious rabies, is not difficult. Observing it in the home, in a veterinary hospital or in an antirabies clinic is not difficult either. In the home a deep verandah, a long strong rope which can be doubled (a clothes-line will do) and plenty of phenyle are all that is necessary. If the dog turns out to be definitely rabid it can be held in the middle of the long rope made taut and tied to two posts or pegs. It can even be taken out for a limited stroll between two men.

#### IV. Mongooses and bats as carriers of rabies

When attention was drawn to rabies in the mongoose in India (Greval, 1932, 1933) it was stated that, according to Blanford (1891), *Herpestes* Illiger was the only generic type known within the Indian area; he recognized eight species. For a time the generic name *Herpestes* Illig. was replaced by *Mongos*, Geof. and Cuv. and all Indian mongooses were referred to it (Wroughton, 1918), but later *Herpestes* was again revived for the Indian forms (Thomas, 1921). At present, ten species and ten varieties of Indian mongooses are recognized (Wroughton, 1918, 1921; Thomas, 1921). In South Africa at that time the yellow mongoose, *Cynictus penicellata*, was taken to be the sole transmitter of rabies (McKendrick, 1931).

Attention was drawn to bats as carriers of rabies in Trinidad in the same year (McKendrick, 1932) and more detailed information made available four years later (McKendrick, 1936). The vampire bats *Desmodus rufus* and *D. rotundus* are the species so far incriminated. 'The possible relation of fruit-eating and other bats in the spread of the disease appears to require further investigation'.

A disconcerting observation made on the bats is that 'four *Desmodus* bats after inoculation with bovine rabies virus, though showing no symptoms of rabies themselves, were capable of transmitting the infection to twenty-four healthy cattle within one to four months after experimental inoculation. One such bat, killed after five months, was proved to have its salivary glands infected'.

A still more disconcerting observation (McKendrick, 1937) is that the bats may recover from furious rabies (not dumb rabies or after paralysis has set in) and become carriers.

Bats of the genus *Desmodus* Wied. are confined to tropical America and South Mexico (Weber, 1928). Bats or Chiroptera of the Indian area have been revised in the *Journal of*

(Continued at foot of next column)

## HORMONES IN MENSTRUATION AND PREGNANCY

PHYSIOLOGY, PATHOLOGY AND TREATMENT—A

RÉSUMÉ

By A. P. PILLAY, O.B.E., M.B., B.S.

Bombay

THE theories regarding the rôle of hormones in menstruation and pregnancy current in former

(Continued from previous column)

the Bombay Natural History Society (Wroughton, 1918). Forty genera and 123 species, excluding subspecies and varieties, of bats are known from the Indian limits.

#### An acknowledgment

For up-to-date information on mongooses and bats the writers are indebted to Dr. Bains Prashad, D.Sc., F.R.S.E., Director, Zoological Survey of India, Calcutta.

#### Summary

1. A dog suffering from chill presented for a whole day the picture of a dog suffering from rabies. Three other dogs presenting the same symptoms are cited. All recovered.

2. Close contact with a suspicious dog like the ones described should be followed by prophylactic antirabies treatment if nothing further were known about the dog.

3. Isolation with a view to observation of the suspected dog, for making sure of the diagnosis of rabies, is much to be preferred to destruction of the dog.

4. Mongooses and bats can carry rabies.

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years were found to be untenable in the light of extensive and more elaborate researches which became possible after synthetization of these hormones. The controversies as to the methods of action of hormones are still raging and often the conclusions of one group of research workers clash with those of others. The result is that a close student of the science of endocrinology is bewildered by the mass of data thrown at him. With all this, certain salient points stand out of these discussions as established facts and suggest new or modified lines of treatment in disorders of menstruation and pregnancy. It is thought that a résumé of these facts will be of practical help to practitioners who have neither time nor facilities to wade through voluminous medical literature.

#### *The sex hormones*

The hormones that are believed to be concerned with the physiological sex functions of women are those of the ovary, anterior pituitary, adrenal and thyroid. There was a time when thyroid products were used extensively in functional sex disorders of the female but their use was empirical and is now almost given up.

Our knowledge regarding the adrenal cortex hormone is still meagre. It is known, however, that hypersecretion of this hormone gives rise to virilism and the hypomenorrhœa, amenorrhœa, and sterility associated with it, while its deficiency causes Addison's disease. Chemically this hormone closely resembles progesterone and biologically, it is believed, to have actions more or less similar to progesterone and the male sex hormone.

#### *The anterior pituitary hormones*

The anterior pituitary gland is known to secrete at least a dozen hormones which control in some way or other all endocrine and non-endocrine organs of the body. The hormone that is concerned with menstruation and pregnancy is prolactin and this is believed to be two, or to have two functions, follicle-stimulating and luteinizing. There is another hormone, prolactin, the lactogenic hormone, which is concerned with the secretion of milk in the breasts during the later stages of pregnancy and the post-partum period.

While prolactin is the anterior pituitary hormone proper, anterior-pituitary-like hormones, or gonadotropic hormones as they are called, have been isolated from the urine and blood serum of pregnant women and mares. No synthetic products of these hormones are available.

Attempts to reproduce artificial menstrual cycles with prolactin and gonadotropic hormones have been successful in laboratory animals but not in human females. The present belief is that the anterior pituitary is not directly or actively responsible for causing menstruation (Engle, 1939). Clinical administration of gonadotropic substances has also met with very little therapeutic success (Davis and Koff, 1938).

It is not denied that prolactin and the gonadotropic hormones, especially those prepared from the serum of pregnant mares and believed to be very potent, may have their place in the treatment of developmental defects, but even here their practical applicability has not yet been clearly defined. The concepts regarding the anterior pituitary hormones are changing daily. On the other hand, our knowledge of ovarian hormones is now so definite that, as Corner (1939) says, the menstrual cycle can be successfully initiated whenever we desire, with no other armament than a syringe and a few ampoules of ovarian hormones.

#### *Ovarian hormones*

The two ovarian hormones known, and synthesized so far, are the follicular hormone, œstrin, and the luteal hormone, progesterone. Œstrin is present in the blood of young girls as early as the age of eight (Fluhmann and Murphy, 1939) and is therefore believed to be secreted even by immature ovaries.

Progesterone, on the other hand, is secreted by the corpus luteum and the formation of this begins only at puberty.

At the time of puberty the ovaries begin to secrete increasingly large quantities of œstrin, and this under the stimulus of the anterior pituitary hormone causes ripening of a Graafian follicle, its rupture and liberation of an ovum. This process, known as ovulation, occurs at about the middle of the inter-menstrual period. The empty follicle now becomes a corpus luteum. Ovulation and corpus luteum formation occur cyclically every month. The corpus luteum begins to secrete progesterone from about twenty-four to thirty-six hours after its formation and continues to do so for the next ten or twelve days, when it retrogresses. About forty-eight hours after the retrogression of the corpus luteum, menstrual bleeding begins.

While the secretion of progesterone is cyclic or periodic, the secretion of œstrin is continuous, first by the follicle and later by the corpus luteum. Recent researches have shown that the corpus luteum secretes a larger quantity of œstrin than even the Graafian follicle. In other words, the aggregate amount of œstrin present in the system is greater during the second half of the menstrual cycle than in the first half (Neustaedter, 1939).

#### *The physiology of menstruation*

It was once believed that menstruation was induced by the corpus luteum 'by some positive effect on the uterus, its presence and activity building up the endometrium to a hæmorrhagic phase'. It is now known that the corpus luteum acts in quite a different way. The menstrual cycle has two phases, the follicular phase and the luteal phase, so called because the follicular hormone and luteal hormone respectively are in control during these phases. The follicular phase starts from the beginning of the menstrual



flow till ovulation occurs and the luteal phase from the time the corpus luteum begins to secrete progesterone to the onset of the menstrual bleeding.

The function of œstrin is not only to ripen the Graafian follicle and cause ovulation but also to inhibit or hold in check menstruation, which does not occur as long as this hormone circulates in the system in sufficiently high amounts. Progesterone checks this menstruation-inhibiting property of œstrin and itself inhibits menstruation. When the corpus luteum, which has been secreting progesterone and œstrin, undergoes retrogression, the woman is suddenly deprived of the inhibiting actions of both œstrin and progesterone and the endometrium breaks down and menstruation ensues.

The uterus will not bleed during the first half of the cycle because the follicle is furnishing the menstruation-inhibiting œstrin and it will not bleed during the second half because the corpus luteum is furnishing progesterone, another menstruation-inhibiting hormone. It has also been proved that total deprivation of œstrin is not necessary to produce menstruation, but merely lowering its level is enough for the purpose.

#### *Non-pathological varieties of menstruation*

*Anovulatory menstruation.*—It is now well recognized that anovulatory types of menstruation are fairly frequent at puberty, at the menopause and in the post-partum period. In women of the child-bearing period, this type of menstruation is seen associated with sterility and amenorrhœa. According to Rock, Bartlett and Matson (1939), 'Sterility patients with a history of menstrual irregularities, even though flowing normally at the time of examination, should arouse suspicion of anovulatory menstruation, since such a failure of ovulation is three to nine times more frequent among these patients than among those whose menstrual history is normal'.

Anovulatory menstruations cannot be explained by the usual œstrin-progesterone-deprivation theory, since there is no formation of corpus luteum in their cycles. Some gynaecologists do not consider anovulatory menstruation as normal menstruation, but this attitude is wrong, as the one resembles the other in every way except in the absence of corpus luteum, and in bleeding taking place in one from a proliferative mucosa, and in the other from a progestationally transformed mucous membrane. The women are in good general health, only they will not conceive.

This type of menstruation proves that corpus luteum is not essential for producing menstruation. Fluctuations in œstrin level in these cases are caused cyclically, it is believed, as a result of the give and take of the pituitary-ovarian or pituitary-ovarian-adrenal relationship; or by the action of some, as yet unrecognized, progesterone or androgen-like hormones produced in the ovary (Corner, *loc. cit.*). Or it may be caused by the action of prolactin. These are all mere

speculation. No statistics as to the relative frequency of anovulatory and ovulatory menstruations are available, but during the course of my investigations on vitamin C and ovulation, I found seven cases of anovulation in twenty-six cycles tested. The ages of the women ranged from fifteen to thirty-six.

Anovulatory types of menstruation are important only as a cause of sterility. The treatment for the condition is by injections of œstrin, as it is deficiency of follicular hormone that causes anovulation. Some gynaecologists advocate gonadotropic hormones. My experience of three cases is that a single injection of 10,000 to 20,000 units of œstrin on the eleventh day of a cycle usually brings on ovulation. The difficulty in checking the efficacy of any treatment is because anovulatory menstruation often alternates with ovulatory menstruation in the same woman, and so whether ovulation in any cycle is natural or produced by the treatment cannot be determined.

*Multiple ovulations.*—By the term multiple ovulations is meant not the simultaneous development and liberation of more than one ovum during a menstrual cycle, but two or more ovulations occurring on different days in a cycle. They are caused by an excess of follicular hormone production but it is not known as to whether these have any adverse effects on the health of the woman or on her fecundity. Hartman (1939) and his colleagues believe that multiple ovulations are not unusual in women during the child-bearing period. During my vitamin-C tests, I came across two cases of multiple ovulations, one alternating with anovulation and another with the usual uniovulation (Pillay, 1940).

#### *Physiology of pregnancy*

The ovum is liberated every month at about the mid-menstrual period and the present belief is that it is capable of fertilization only for twenty-four or forty-eight hours after its liberation. If within this time it meets a spermatozoon it is fertilized, otherwise it is discharged with the menstrual flow. Embryologists are now definite that the time the ovum, when fertilized, takes to migrate from the fallopian tube to the uterus and get implanted is about ten days, *i.e.*, within the period during which progesterone is secreted by the corpus luteum. For the implantation of the ovum, progesterone is known to be essential. If for any reason the corpus luteum does not secrete a sufficient quantity of progesterone or secretes it only for less than the usual ten or twelve days, implantation of the ovum will not take place. This means degeneration of the endometrium, and the discharge of the fertilized ovum in the resulting menstruation.

It was once thought that progesterone was necessary only in the early stages of pregnancy. This was based on the observations that the corpus luteum degenerated at about the third



month of conception and that pregnancy continued even if the ovaries were removed by operation after the third month.

It has now been definitely established that progesterone is necessary right through pregnancy. For about the first three months the ovaries supply progesterone and then they retrogress. The function of producing progesterone is now taken up by the placenta. The exact time when the transference of this function from the ovaries to the placenta takes place varies in different women and in the same woman in different pregnancies. It is believed to be somewhere between the seventieth and ninetieth days, counting from the first day of the last actual menstruation.

If the corpus luteum fails to secrete a sufficiency of progesterone for any length of time before the placenta begins to secrete it, abortion will result. This is most likely to occur near the time of the transference of the function of progesterone secretion from the ovaries to the placenta and this period is therefore the most critical in pregnancy. It has been recognized for a long time that abortion tends to occur most commonly about the third month, i.e., by our assumption just before the placenta takes over progesterone production. Henry, Venning and Browne (1938) studied the distribution of time of onset of symptoms in five hundred cases of abortion (threatened, complete and incomplete) and found the average day to be the eighty-first from the beginning of the last menstrual period.

In normal pregnancy, the level of progesterone rises from the time the placenta begins secreting it and continues rising up to term. When the placenta separates during labour, progesterone disappears from the system.

Œstrin and prolactin are also present during the whole term of pregnancy. Œstrin, like progesterone, is secreted in the ovary in the first three months, and later by the placenta in increasing quantities. Prolactin is secreted by the chorion from the time of implantation of the ovum up to term in varying quantities. At the time of parturition, all the three hormones disappear from the system. The rôle of anterior pituitary hormones in the physiology of normal gestation has not been definitely ascertained, but it is believed that they play an important part in keeping up the functional integrity of the corpus luteum of pregnancy and later in the placenta's elaboration of progesterone and Œstrin.

'All the factors involved in the initiation of labour have not been ascertained but quantitative studies in women have revealed a marked drop in Œstrin just before delivery and a decrease in progesterone has also been indicated. It is also seen that there is an increase of prolactin before labour begins. The drop and increase appear to take place suddenly' (Smith and Smith, 1939).

The presence of the various hormones in the system and the quantities present are ascertained by testing the blood or urine for their

excretion products, pregnandiol for progesterone and œstrogens for œstrin. Prolactin appears as prolactin. According to Wilson, Randall and Osterberg (1939), 'the excretion of pregnandiol in normal or maximal amounts in the urine of a woman who has missed her period and who has had a normal menstrual history is apparently indicative of early gestation'. The excretion of prolactin from the very early stages of conception is made use of in the well-known Zondek-Ashheim test of pregnancy.

*Puberty.*—There is one factor common in both puberty and menopause and that is a deficient secretion of œstrin. Anovulation is also common during these periods. While a great amount of scientific work has been done on the menopause, puberty seems to have been neglected, since it seldom gives rise to serious symptoms. The conditions that need medical attention during puberty, as far as the sex functions are concerned, are genital infantilism and hypomenorrhœa. The rational treatment in both cases is by œstrin. Hypomenorrhœa gives rise to much anxiety in parents but usually it needs no treatment as menstruation will get regularized when the girl grows older. Œstrin orally, about 3,000 to 10,000 units daily for the first ten days in the follicular phase for two or three cycles, would be all the treatment that would be usually required.

Genital infantilism may need injections of œstrin and, according to some, of prolactin and gonadotropic hormones. In this and other cases of genital dysfunction, it is better to try œstrin first and if this does not give relief, anterior pituitary hormones.

### Menopause

The theories regarding the causation of menopause are varied and conflicting, but two facts stand out clearly from them. These are that there is an excess of production of gonadotropic hormones and that there is some dysfunction of the ovaries causing deficiency of œstrin and absence of ovulation. According to Fluhmann and Murphy (*loc. cit.*), the deficiency in œstrin is not the primary factor concerned in the production of climacteric symptoms, but it is the presence of excessive amounts of gonadotropic substances that cause them.

Whatever the causation of the symptoms may be, all clinicians are agreed that œstrin administration is the correct treatment in menopause. The dosage of œstrin is important. Schneider (1939) gives the following method for deciding accurate dosage. The correct dose is that amount that would give relief, even though only transitory, within an hour after giving the injection. He begins with an initial injection of 500 international units and the strength of the daily injection is increased until the minimal amount which gives relief within an hour is ascertained. This dosage, in his experience, rarely exceeds 10,000 units a day and upon its determination, the patient is put on oral therapy. The dosage

orally will be three times the ascertained minimal injection dose, given in divided doses.

Recently, testosterone propionate has been used to relieve menopausal symptoms. The male hormone is believed to act by depressing pituitary gonadotropic secretion. Treatment is commenced with an initial injection of 10 mg. of testosterone propionate, the subsequent doses and their frequency being decided by the reaction on the symptoms. It has to be borne in mind that we can expect relief of the physical and mental symptoms in menopausal women, only if these are caused by the menopausal condition itself.

#### *Abnormalities of menstruation*

*Diagnosis.*—Before going into the abnormalities of menstruation and pregnancy, a word might be said about the question of diagnosis. Functional menstrual and pregnancy disorders are due to deficiency or absence of particular hormones or upsets in the relative levels of the various hormones. Accurate diagnosis is essential not only to ascertain which particular hormone is deficient or absent, but also to decide on the optimum dose in treatment. For this, hormone assays of urine or blood are necessary.

As Campbell and Sevringhaus (1939) say :— 'We are still of the opinion that diagnoses as to the cause of amenorrhœa, irregular menses, menorrhagia, and sterility cannot be made by any combination of history taking, physical examination and pelvic examination, or with ordinary laboratory tests. The use of the microscopic study of endometrium, or at times of the vaginal epithelium and the pregnandiol excretion give information of prime importance. Without such data diagnoses are inaccurate, and therapy is empirical. Such examinations are to precede the use of expensive and potent endocrine materials. To determine progress, the history of menstrual flowing is likewise inadequate, unless fortified with similar examinations'. In many cases, œstrogen and prolan assays will also be necessary.

*Amenorrhœa.*—Amenorrhœa is a very wide term and under it are included conditions ranging from the complete absence of menstruation to the prolonging of the menstrual cycle and even a scanty flow. *Ætiologically* it is classified as primary or secondary, the difference being that in primary amenorrhœa, the woman has never menstruated, while in the secondary variety, amenorrhœa sets in after she has menstruated for a certain number of years. It may also be complete or relative. Both types of amenorrhœa are caused by deficiency or defective functioning of either of the ovarian hormones. Relative amenorrhœa is not unusual at puberty, during menopause and in virilism. In the latter condition, it is caused, as was mentioned, by an excess of adrenal cortex hormone which appears to have an antagonistic action on œstrin. The treatment of virilism, so far unsatisfactory, has been

with injections of œstrin. In one case of secondary virilism, I administered by injection and orally 100 mg. of œstrin, i.e., 1,000,000 units in two menstrual cycles. This appeared to regularize her 'returns'. Another 150 mg. were given in the next menstrual cycle and this delayed her 'returns' for fifty-three days. Even these massive doses made no impression on the patient's hirsuties.

*Primary amenorrhœa.*—Primary amenorrhœa is usually associated with genital infantilism or hypoplasia, though cases in which the genital organs are apparently normal are also seen. The aim of treatment is to bring on full physical and functional development of the ovaries and uterus. This is believed to be a good field for prolan, if genital hypoplasia is associated with general infantilism, otherwise œstrin is the hormone to be exhibited. Even in the former case, after the course of prolan, œstrin alone or with progesterone in sequence may have to be given.

From the year 1933, when Kaufmann succeeded for the first time in inducing menstruation in a human female castrate by the administration in sequence of œstrin in the follicular phase and progesterone in the luteal phase, this procedure has been adopted as the routine treatment in all cases of amenorrhœa whether primary or secondary. *œstrin* was not administered in the luteal phase under the mistaken belief that there was no production of this hormone by the corpus luteum. To imitate what is occurring in the system, œstrin has to be administered continuously and, during the later stages of this treatment, progesterone is given for about ten days.

The conclusions summarized by Engle (*loc. cit.*) from researches of various workers to date will be most helpful to understand this and other recent therapeutic approaches in menstrual disorders.

1. Withdrawal or reduction of œstrin level results in typical uterine bleeding.

2. Bleeding of œstrin deprivation will not occur if, after œstrin, progesterone is given.

3. After a course of progesterone, however, bleeding *always* occurs after its withdrawal, even if the progesterone injections are followed by injections of œstrin in heavy doses.

4. *œstrin* and progesterone are not antagonistic in their action but are essentially synergistic.

5. The time interval between hormone withdrawal and bleeding is characteristic for each hormone. The onset of bleeding after œstrin withdrawal is 9.2 days, with a range of five to sixteen days. After cessation of progesterone therapy, bleeding occurs on the average of 2.9 days, with a range of two to four days. This is shorter and more constant than after œstrin withdrawal.

6. The real third or pre-menstrual phase is only forty-eight hours or less, when both the

ovarian hormones are not acting on the endometrium.

The rational treatment for primary amenorrhœa is therefore as follows : As the patient has never menstruated, an arbitrary period is fixed as the menstrual cycle. Daily injections of œstrin, 10,000 units, are given from the first day right through the cycle. From the thirteenth day progesterone, 10 mg. doses, is given daily for ten days and stopped. Menstruation may reasonably be expected two to four days after the stoppage of progesterone injections. In long standing and severe cases the treatment is kept up for another two or three cycles.

*Secondary amenorrhœa.*—Secondary amenorrhœa is believed to be caused by the absence of, or a defective corpus luteum, in other words, by having no progesterone to act on œstrin which is continuously produced in the follicle. Two lines of treatment are possible. One is by administering œstrin and producing corpus luteum and the other is by supplying progesterone by injections. As was mentioned, the line of treatment that was being adopted till recently was giving œstrin and progesterone in sequence or œstrin alone in the follicular phase.

Zondek and Rozin (1939) utilized the progesterone-withdrawal principle to initiate uterine hæmorrhage in secondary amenorrhœa, treatment being this hormone alone without preliminary treatment with œstrin. They gave daily injections of progesterone, 10 mg. for five days, and found that bleeding set in sixty hours after the last injection, and the blood discharged resembled menstrual blood in that it did not coagulate. Similar results were obtained by them also by the oral administration of pregneninol, a derivative of progesterone. The oral dose found effective is 300 mg. in five days, i.e., six times the dose of progesterone when given by injection. I have been practising this line of treatment with excellent results. I give 60 mg. by injection in four daily doses of 15 mg. and the bleeding comes on from forty to seventy-five hours after the last injection. The conclusion of Zondek and Rozin that uterine bleeding started in all cases exactly after sixty hours does not appear to be correct in my experience. Doses below 10 mg. of progesterone appear to be ineffective.

One case is worth reporting in detail as it shows the comparative merits of œstrin-progesterone therapy and progesterone therapy alone.

A Hindu woman, age 35, married. Very irregular for the last four years, menses every four or five months and recently none at all. From 6th to 16th June, 1939, she had 20 mg. of œstrin in four doses and from 21st to 26th, 6 mg. of progesterone in three doses. On 28th she had a slight flow for a few hours. On 4th July treatment was resumed and till 15th, she had 25 mg. of œstrin in five doses and from 24th to 26th July, she had daily injections of 5 mg. of progesterone. On 31st July, she got her returns and this lasted for two days.

She had no other menstruation after that. From 8th March, 1940, she was given daily 15 mg. of progesterone by injection for four days and on the fifth day she

was given only 10 mg. The last injection was given at 9 a.m. on 12th, and she got her returns, not very satisfactory, according to her, at 5 a.m. on 16th March, i.e., ninety-two hours later. The œstrin-progesterone treatment took fifty-six days to show results while progesterone therapy took only nine days.

Absence or even delayed menstruation causes great mental depression in women. With progesterone therapy the doctor can guarantee the menstrual flow within two to four days after the cessation of the treatment, while with œstrin therapy, the result takes about three weeks to appear and no definite date can be guaranteed. Then again progesterone therapy is cheaper and more scientific than Kaufmann's method which is being followed at present. In the old œstrin-progesterone treatment, œstrin was a waste as the uterine bleeding would have been initiated by the progesterone alone. According to Zondek and Rozin (*loc. cit.*) the progesterone treatment is not effective in primary amenorrhœa and 'this reveals a characteristic difference between primary and secondary amenorrhœa'.

*Oligomenorrhœa and hypomenorrhœa.*—Oligomenorrhœa and hypomenorrhœa should be included under amenorrhœa. These conditions are generally associated with hypoplasia genitalis and so œstrin treatment is indicated. Hypomenorrhœa has already been described. I have seen excellent results in oligomenorrhœa by a single injection of œstrin, 5 mg., on the eleventh day of the cycle, repeated in two or three subsequent cycles. Ogino has laid down that the one constant feature in all menstrual cycles is that menstrual bleeding takes place on the fifteenth day after ovulation. This seems to be well established, as hypomenorrhœa and other conditions where the menstrual cycle is unduly prolonged, can be brought to the normal type only by shortening the pre-ovulation period. Medication by œstrin to shorten the cycle should therefore be undertaken in the pre-ovulatory period. Œstrin administered in the luteal phase has no effect on the cycle. Progesterone on the other hand can bring on menstruation as and when required.

*Post-coital amenorrhœa.*—There is another form of amenorrhœa which may be called, for want of a better name, post-coital amenorrhœa. It is seen in married women and unmarried girls who have been menstruating regularly but who though they dread pregnancy had exposed themselves to it. This amenorrhœa is not caused by pregnancy, nor can it be considered as pseudo-pregnancy, as there are no other subjective symptoms associated with it. This form of amenorrhœa is due probably to some psychic inhibition of the ovarian function. That coitus plays a part in ovarian functioning is seen from the fact that it initiates ovulation in rabbits probably by some psychic reaction on the pituitary-ovary relationship. Though ovulation in the human female is not influenced by coitus, it apparently suppresses menstruation at least temporarily, by the psychic factors, fear and anxiety.

I selected for progesterone treatment five such cases, one unmarried and four married, who had exposed themselves to becoming pregnant. The menstruation was overdue by six, nine, fourteen, fifteen and twenty-eight days respectively. The first four cases had 60 mg. in four days, and the fifth 75 mg. in five days. The first four women had their menstrual flow, ninety-six, sixty-nine, forty and seventy hours after the last injection, while in the fifth case the treatment was a failure. This case turned out to be a case of pregnancy.

The first case is interesting :—

Married woman with seven children and a fear of pregnancy. She had daily injections of progesterone 15 mg. for four days and the fourth injection was given on 30th January at 12 noon. As she had no flow till 10 a.m. on the 3rd February, she induced me to start œstrin treatment the same morning and was given 14 mg. of œstrin, i.e., 140,000 units. An hour later, she got her returns but this she hid from me as she wanted a good 'flush out'. Twenty-three mg. or 230,000 units were given in the next two days. The flow, which usually lasted only three days, went on this time for twelve days. This case goes to prove the conclusion that œstrin administered after progesterone does not inhibit menstruation even in high doses.

Progesterone is thus seen to initiate menstrual bleeding in post-coital amenorrhœa if it is not due to pregnancy. The treatment may be used therefore as a diagnostic test for early pregnancy when other tests are not feasible. It was mentioned before that presence of pregnandiol in the urine of a woman who missed a period but who was menstruating regularly previously is also a test for pregnancy. All the cases in my series required only one course of treatment and they had so far two and three returns after the cessation of the treatment. I have treated successfully similar cases formerly with daily injections of 50,000 to 100,000 units of œstrin for three to five days. Menstruation came on all right but not before eight to twelve days after the last injection.

*Menorrhagia and metrorrhagia.*—The theory of the causation of menstruation described in this paper makes it possible to believe that pathological uterine bleeding is also caused by fluctuations in levels of ovarian hormones and that no sharp distinction exists between them and menstruation proper (Corner, *loc. cit.*).

Excessive bleeding indicates either low levels of œstrin and/or deficient functioning of the corpus luteum. By the theory we enunciated, viz, that as long as œstrin circulated in the system in sufficiently high levels uterine bleeding was inhibited and that progesterone also suppressed menstruation, treatment of menorrhagia and metrorrhagia can be by the administration of œstrin or by progesterone. Œstrin would appear to be the scientific way of treatment as it raises the œstrin level in the body and also induces corpus luteum formation. If the bleeding is excessive when the patient comes for treatment, progesterone in high doses is to be administered. After bleeding stops, œstrin

and progesterone together or in sequence should be given just as in amenorrhœa. In these cases, urine assays will be helpful in deciding which hormone to exhibit.

It is assumed that cancer, tumours and similar other causes of uterine bleeding have been excluded before hormone treatment is begun. Some gynaecologists advocate anterior pituitary hormones for uterine hæmorrhages, some recommending prolactin and others gonadotropic hormones, most preferring preparations from the serum of pregnant mares as these are believed to be more potent than the others.

The recent organotherapeutic development in the treatment of functional uterine bleeding has been the administration of the male hormone, testosterone propionate. As was mentioned, this product is believed to act through its inhibiting effect on the pituitary. Biologically, while testosterone is antagonistic to œstrin, it has the same action as progesterone in preventing œstrin-withdrawal bleeding even in doses of 5 mg. (Engle, *loc. cit.*). I have noticed immediate and spectacular results in functional bleeding by the combined use of testosterone propionate, 25 mg. and progesterone, 10 mg. It was mentioned that adrenal cortex hormone has similar actions as progesterone and testosterone and therefore it should prove useful in excessive uterine bleeding. There are however no recorded studies on the subject.

*Dysmenorrhœa.*—Dysmenorrhœa is the commonest menstrual disorder and yet very little is known about its causation and its treatment is still unsatisfactory. There are three current theories as regards its ætiology and these are :— (1) deficiency in progesterone, permitting the unopposed action of œstrin upon the uterine muscle; (2) excessive œstrin production causing violent contractions of the uterine muscle; (3) excessive progesterone activity. It is very probable that there is also some nervous element in the causation of dysmenorrhœa.

Till recently, the treatment consisted of injections of œstrin in the first half of the menstrual cycle and of progesterone in the premenstrual week. These were given more or less empirically and so some cases were benefited, while others were not.

Recently other methods of treatment have come into vogue. The most important of these is by testosterone propionate. It was mentioned that this substance inhibits the gonadotropic factors of the pituitary. It causes suppression of œstrin, ovulation and progesterone formation. Large doses of testosterone propionate suppress the subsequent menstruation if given in the follicular phase, but not when given in the luteal phase. Injections of 25 mg., three times a week, in the luteal phase of the menstrual cycle, give excellent results in dysmenorrhœa. One or two courses will be found ample. Testosterone propionate relieves also the discomfort, pain and swelling in the breasts seen in the luteal phase of

the menstrual cycle of some women. The male hormone should, however, be used with caution in women as doses over 500 mg. in one cycle may give rise to signs of masculinization, such as hoarseness of voice, facial hirsuties, suppression of menstruation and so on (Salmon, Geist and Walter, 1939).

Alitchul found small doses of insulin effective in dysmenorrhœa. Schrick (1939) suggests two alternative ways of administering insulin, five units daily before lunch for three to five days before the menstrual period, or a single injection of five to seven units given during the attack. I have seen in two cases relief of pain within fifteen minutes by a single injection of fifteen units given during the attack.

I had also good results, though not so spectacular as with insulin or so lasting as with testosterone propionate, with Benerva (vitamin B<sub>1</sub>) injections, and with vitamin D by injection and orally. Whether these products are really effective is difficult to say, as it is almost impossible to eliminate the psychic element from the therapeutic results obtained in the treatment of dysmenorrhœa.

#### *Abnormal conditions seen during pregnancy*

Very little is known about the endocrine or other causation of abnormal conditions occurring during pregnancy, except that in pre-eclampsia and other late toxæmias, a rise in prolactin level and a drop in œstrin level are noticed. What usually happens in normal pregnancy is, that from the time of implantation of the ovum, the chorion secretes large quantities of prolactin. A rapid decline in its level takes place during the third and fourth months. This decline coincides with the taking over by the placenta of the functions of the regressing corpus luteum. The low level of prolactin is maintained during the fifth, sixth and seventh months during which time the production of œstrin and progesterone steadily increases. Any upset in the normal levels of prolactin and œstrin in these months would give rise to toxæmias of pregnancy. It is also believed that there is some involvement of the adrenal cortex in these toxæmias. In all cases of abnormalities of pregnancy, a test for prolactin estimation should be done. Excellent results have been reported by treatment of such conditions by œstrin and by progesterone.

*Abortion.*—The causes of spontaneous abortion are many but here we are concerned only with its endocrine aspects. From the previous pages it will be clear that deficiency of progesterone and a short phase of corpus luteum are the usual endocrine causes of abortion. Abortion is therefore most likely to occur in the periods between fertilization of the ovum and its implantation in the uterus and just before the placenta takes over the progesterone-producing function from the regressing corpus luteum. That is to say, the danger periods in pregnancy

are the first ten days and the third month after fertilization of the ovum.

Progesterone therapy is the only possible method of treatment in abortion, though, from my limited series of cases, I am of opinion that better results are obtained in threatened abortion by combining testosterone with progesterone. The dosage of progesterone necessary to maintain pregnancy intact in the human being is difficult to determine. According to Browne, Henry and Venning (1939): 'From the pregnandiol assay, it seems obvious that the amount of progesterone produced by the corpus luteum up to the seventieth or eightieth day is 5 to 10 mg. per day, and that the placenta produces a gradually increasing amount as pregnancy advances. How much is the minimum requirement is unknown. It is also unknown, unless determinations are made, how much the patient's own endocrine organs are producing, so that one may be giving 1 mg. of progesterone to a patient in the fourth or fifth month, when she is producing 25 to 50 mg. herself. In any case, it would seem, in view of the above findings, that doses of less than 5 mg. are unlikely to have much effect. This dose should be given daily or every other day, and may be increased in the presence of persisting symptoms. In most cases, either of the threatened or habitual type, therapy should be concentrated during the period of transfer of the function of formation of progesterone from ovary to placenta, since it is at this time that abortion is most likely to occur. If pregnandiol assays are available a definite rise in pregnandiol excretion may be taken as an index that further therapy is probably unnecessary. The danger of wasting treatment on an already dead fetus, and the uselessness of treating a patient after her own placenta has begun to form normal amounts of progesterone, should always be borne in mind'.

The vexed question as to whether hormones can produce abortion has been answered differently by different observers. Some say that it is possible, while others say that it is not. From the theories so far discussed it is clear that theoretically it should be possible to produce abortion in the early stages of pregnancy by the use of œstrin. To me it appears that it would be also practicable during the danger periods of pregnancy, provided it can be decided how much œstrin is required to 'neutralize' the amount of progesterone that is being secreted by the patient's endocrines. Water-soluble products of the follicular hormone act better because of their quicker absorption. It may be mentioned that œstrin has the property of sensitizing the uterus to the action of oxytocic drugs and to local interference. Progesterone has just the opposite action.

*Sterility.*—It is not proposed to go into the causes or treatment of female sterility in detail except to mention one or two endocrine aspects of the subject. A short phase of corpus luteum



activity, as was mentioned, does not permit the implantation of the ovum in the uterus and is one of the usual but neglected causes of sterility. In these cases it is necessary to give as a precautionary measure 5 mg. doses of progesterone by injection daily, from the seventh to the tenth day after a mid-cycle coitus. In habitual abortion, 5 mg. doses of progesterone should be given at least every other day for the first three months.

Another common cause of sterility, and one to which also very little attention is paid, is anovulation. To detect this, an accurate test for ovulation is required. The vitamin-C test I formulated, if found reliable, is simple and can be carried out even by the general practitioner. There is increasing evidence that anovulation, like aspermia, is more common than is usually believed to be possible. The treatment for anovulation has already been described as injections of œstrin.

#### *Mode of administration of hormones*

The synthetic preparations of hormones now available can be administered, unlike the previous natural products, in various ways, such as by injection, orally, percutaneously, through the vagina and by subcutaneous implantation. Injections give the most rapid results and subcutaneous implantation the most sustained. Percutaneous application is claimed to be nearly as effective as injection. Orally five or six times the injection dose are required. I found application of greasy ointments to the skin far too messy and, so in males, I have been prescribing them with good results rectally. This method of administration is not mentioned in any literature and I feel that there will be better absorption if the base used in the preparation of the applications is glycerine-starch instead of vaseline. For subcutaneous implantation, a compressed tablet of the crystalline hormone of the required weight is sterilized in an autoclave and inserted under the skin through a small incision which is then sutured.

In this paper, I did not think it necessary to confuse issues by entering into a discussion of the different chemical products of the various hormones available. There may be slight variations in the degree of efficacy and in the rapidity of action, but these are of minor importance in hormone therapy. The propionates are believed to be more lasting in their effects than the other products. Opinions are divided as to the permanency of the results of hormone treatment. Unless the cause is definitely ascertained and the dose accurately decided, results are bound to be temporary. This is probably why many cases of primary amenorrhœa relapse when treatment is discontinued. The only bad results I have noticed in women, even after giving enormous doses of hormones, were masculinization when the male hormone was administered and the delayed menstruation in the virilism case reported above. The fear that

prolonged use of hormones may cause cancer seems to be unfounded.

#### *Summary*

The œstrin-deprivation, the progesterone-deprivation and the œstrin-progesterone-deprivation theories of menstruation are explained. These make it necessary to rearrange many of our views regarding the rôle of hormones in the physiology and pathology of menstruation. They also make it possible for us to believe that there is very little difference between normal menstruation and pathological functional uterine bleedings and that the treatment of the latter is merely by bringing the œstrin-progesterone level to normal.

It is shown how in amenorrhœa, unassociated with genital hypoplasia, treatment by progesterone is simpler, more rational, and more rapid in effect than œstrin or œstrin-progesterone therapy. The belief that œstrin and progesterone could be given only in sequence and not simultaneously is shown to be groundless. In certain functional disorders their combined use is recommended. The possible causation and treatment of post-coital amenorrhœa is explained.

The recent developments in the use of male sex hormones in functional female disorders are described.

It is shown that to maintain pregnancy intact high and constant levels of progesterone are essential and to prevent abnormal conditions during this period, the normal balance between the ovarian and anterior pituitary hormones has to be maintained.

Abortion and sterility are shown to be similar in the sense that the ætiological endocrine factor behind both is defective progesterone production. Anovulation is considered as common and important a cause of sterility as aspermia.

The effective dosage of hormones and the various methods of administering them are described.

It is emphasized that accurate diagnosis and correct dosage cannot be arrived at without assays of urine or blood for pregnandiol, œstrogen and prolan excretions.

#### *Acknowledgment*

I am indebted to Messrs. Ciba Ltd. and their scientific representative in this country, for placing at my disposal liberal supplies of their hormone products, without which this study would not have been possible.

The products used in this study were :—Follicular Hormone—*Ovocyclin* (ampoules, tablets and ointment); Luteal Hormone—*Lutocyclin* (ampoules and tablets); Male Hormone—*Perandren* (ampoules and ointment); Adrenal Cortex Hormone—*Percorten* (ampoules).

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## A Mirror of Hospital Practice

### A CASE OF BANTI'S DISEASE

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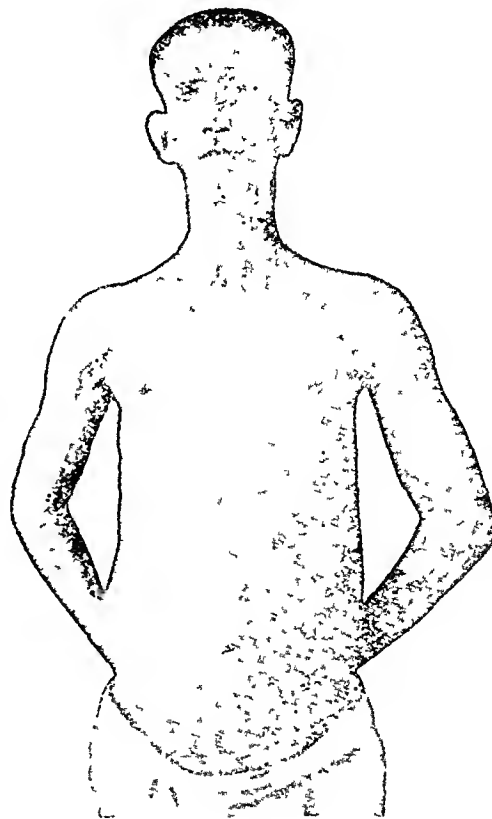
IN the British Isles where the discovery of a large spleen causes a mild sensation, Banti's disease is comparatively rare and is included in the syndrome of splenic anæmia. The diagnosis is largely a matter of eliminating other causes of enlarged spleen and is not very difficult.

In India the position is very different, firstly because enlarged spleens are common, and secondly because the cause of some of these enlarged spleens is unknown.

De (1932) examined several hundred enlarged spleens pathologically and found that in an appreciable number of them there was no evidence of any known disease but that clinically these cases had certain features in common. They were commonest in certain districts of Bengal, and always suffered from an irregular type of fever. Therapeutic measures were futile and a secondary type of anæmia with reduction of leucocytes was constantly present. These cases tended to develop fibrosis of the liver with ultimate cirrhosis and ascites. Death from intercurrent infection such as pneumonia or ulcerative colitis was usual.

The above description bears a close resemblance to Banti's disease as was pointed out in an editorial of the *Indian Medical Gazette* (1935). As a result of further research, De (1938) amplified his previous description and gave details of laboratory tests which included the information that the sedimentation rate was

much increased and the fragility of the red blood corpuscles diminished.



Photograph of the patient soon after admission, showing the outline of the spleen.

The question which confronts the clinician is, are these cases which present the above picture to be diagnosed as belonging to the splenic anæmia syndrome, or are they examples of another disease?

Palit (1935, 1937) described two series of cases on which he performed splenectomy for splenomegaly. Seven of these cases were diagnosed as splenic anæmia or Banti's disease. The term Bengal splenomegaly has been applied by others (Connor, 1933; De and Tribedi, 1939) to this type of case.

If a comparison is made clinically between Bengal splenomegaly and Banti's disease certain differences become apparent

(1) Fever is always present in the former and absent in the latter.

(2) Hæmatemesis occurs in 50 per cent of cases of Banti's disease (Whitby and Britton, 1939) but is rare in Bengal splenomegaly.

(3) The administration of iron produces improvement in Banti's disease (Dunlop *et al.*, 1939) but does not do so in splenomegaly.

(4) The leucopenia described in Banti's disease is marked and constant. In Bengal splenomegaly the leucocyte count is reduced, but moderately so. Some of the cases described (Palit, 1937) exhibited a slight leucocytosis.

(5) Death is commonly due to hæmorrhage in Banti's disease and due to intercurrent infection in Bengal splenomegaly.

We may conclude that Banti's disease in India is comparatively rare, whereas Bengal splenomegaly, which closely resembles it, is common. Failure to differentiate between the two conditions is of little importance as treatment is largely the same for both. Better results appear to follow splenectomy for splenomegaly than for Banti's disease.

A case of Banti's disease was recently admitted to the Presidency General Hospital, some details of which may be of interest.

An Anglo-Indian male aged 48 years complained of breathlessness and swelling of the abdomen. He said that he had not been in good health for the past 24 years. He had managed to keep a boarding house until poor health and finances had made it necessary for him to enter a home.

In the last two years he had become breathless on exertion and felt a dragging pain in the abdomen. The exertion of chopping wood in the home proved too much for him and he reported sick to the home doctor. On questioning he admitted having attacks of hæmatemesis, and on these occasions he used to vomit up a 'chamber pot full of blood'. His weight in 1916 was 12 stone but he had gradually lost weight till he became very thin. Recently his abdomen had swollen up. He had not bled from his nose or gums but his stools had been black sometimes. He did not remember being jaundiced.

On being asked about previous illnesses he recited the following list of hæmorrhages which seemed to have left a very vivid impression on him.

October 1916 hæmatemesis. He vomited a chamber pot full of blood.

1917 hæmatemesis once.

1918 hæmatemesis once.

1919 hæmatemesis once.

1920 hæmatemesis twice in Darjeeling.

1923 hæmatemesis twice in Vizagapatam.

1936 hæmatemesis once in Hyderabad.

1937 hæmatemesis once in Ootacamund.

March 1938 hæmatemesis twice on 4th and 15th in Darjeeling. At the time of hæmatemesis he used to feel faint and then 'up came the blood'.

There was nothing of interest in his family history. He was unmarried and no other member of his family had suffered from hæmorrhages.

On examination it was noted that he was an intelligent man, very thin, with a large abdomen. The spleen was enlarged below the umbilicus and the liver was not palpable. Ascites was present and the superficial abdominal veins were prominent. There was no enlargement of glands. A hæmic murmur was heard on auscultation of the pulmonary area of the heart.

The results of laboratory tests were as follows:—  
Blood—

Red blood corpuscles	..	2,690,000 per c.mm.
Reticulocytes	..	4 per cent.
White blood corpuscles	..	3,120 per c.mm.
Hæmoglobin	..	50 per cent.
Neutrophils	..	57 "
Eosinophils	..	3 "
Lymphocytes	..	34 "
Monocytes	..	6 "

There was a considerable reduction in the platelets.

Gastric analysis.—No free acid present.

Aldehyde and Chopra tests.—Both negative.

Splenic and sternal puncture.—No Leishman-Donovan bodies present.

Wassermann reaction.—Positive.

Blood fragility test.—

Hæmolysis started at 0.48 per cent.

completed at 0.35 per cent.

..

Treatment consisted of the administration of ferrous iron, liver, and a nourishing diet. Dilute hydrochloric acid was given in view of its absence in the gastric juice, and calcium was also given for hæmorrhages. The patient refused to consider splenectomy.

At first some improvement was noted. His red blood corpuscles rose to nearly  $3\frac{1}{2}$  millions and his hæmoglobin to 60 per cent. The white blood corpuscles also increased to 4,500 per c.mm. After two weeks his progress was arrested so he was given urea stibamine and later on arsenical injections (Mapharside).

About a month after admission the abdomen began to increase rapidly. The abdominal veins became very prominent and the spleen, which was hard and firm, floated about in a bag of fluid. His abdomen was tapped and 220 ounces of fluid were drained off slowly. A few days later he had a severe hæmatemesis and passed blood in his stools. Soon he began to pass pure blood in his stools and finally, following another large hæmatemesis, he died.

A post-mortem examination was made. The abdominal cavity was full of free fluid. The spleen which weighed 2 lb. filled a large part of the cavity. The capsule was wrinkled and adherent to the left lobe of the liver and surrounding structures. It was pale and had superficial hæmorrhages. There seemed to be an excess of fibrous tissue. The spleen was smaller than normal and weighed 2½ lb. It was very pale and had hæmorrhages on its surface. There were no obvious nodules but the substance felt hard in places suggesting increased fibrous tissue.

The stomach was full of clotted blood. The veins in the region of the lower end of the œsophagus were markedly enlarged, prominent, and varicose. The inner surface of the œsophagus presented two holes, one larger and one smaller than the head of a pin which communicated with veins.

The small intestine was congested and contained diluted blood. The bone marrow of the right femur was hyperplastic and smears made from it showed a reduction of the granular series of white cells.

Other organs showed no abnormality except the first part of the aorta which was slightly atheromatous.

### Summary

(1) A case of Banti's disease, including post-mortem examination, is described in detail.

(2) The differential diagnosis from Bengal splenomegaly is discussed.

### Acknowledgment

I wish to thank Major J. C. Drummond, I.M.S., Superintendent of the Presidency General Hospital, for permission to report this case.

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\**B.M.J.*, 1937 August 28. Page 412.



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# Indian Medical Gazette

JULY

## MATERNAL MORTALITY IN CALCUTTA

THE strict definition of 'maternal mortality' would be deaths of women for the period of their lives during which they are capable of bearing children, but it is restricted to define the deaths of women directly or indirectly resulting from the functions of pregnancy and childbirth. It is obviously a very important factor in influencing the increase or decrease of a population, and as such it has given rise to much thought and inquiry all over the civilized world.

In India the problem is of extreme gravity and it has been the subject of several investigations in the last decade. Some of the more important of these are the reports by Sir John Megaw in 1933 as the result of a questionnaire, the object of which was to throw light upon certain aspects of public health in villages, among which was the death rate of women from childbirth. Then Dr. Margaret Balfour, working under the Indian Research Fund Association, first investigated the cause of maternal deaths in hospitals, by the study of hospital records all over the country, and later she studied the same problem among tea garden coolie women in a large district in Assam. Since that time the Association of Medical Women in India has continued to collect records of maternal mortality from hospitals. Although these various records are of great value it was thought by the special Advisory Committee on Maternal Mortality appointed by the Indian Research Fund Association that more information should be gathered and so in 1935 it was decided to inaugurate a special inquiry on the mortality among women who gave birth to children in their own homes, as this would add useful information to that already compiled from hospitals. This inquiry was based on the All-India Institute of Hygiene and Public Health in Calcutta, and was conducted for one year 1936-1937. The report of this inquiry has been published recently, and we give elsewhere in this number a short abstract from its pages.

The difficulty of acquiring accurate information on deaths from any cause in India is very great on account of the imperfect system of death registration and certification that exists almost everywhere, and in this report the shortcomings from this cause are taken into account but they seem to be fairly accurate on the whole, as a result of active co-operation of the local health authorities and painstaking system of house visiting by the persons conducting the inquiry.

On the whole the causes of death are similar to those in other parts of the world, and although the total deaths are higher in India, the deaths from sepsis are in about the same proportion as they are in the British Isles and the United States, and are actually slightly lower. This is very surprising when we consider the number of imperfectly-trained *dais* who still conduct a large number of births in this country. The training of midwives is now being actively pursued in many centres in India as so it may be reasonably anticipated that as more and more properly trained women become available this cause of death will be reduced.

The problem of anæmia which, when it was first noted as an important cause of maternal mortality, appeared to be caused by pregnancy *per se*, was stated by Dr. Margaret Balfour to be responsible for half the maternal mortality in the Assam coolie women she investigated. The present report finds that maternal deaths attributable to anæmia in Calcutta are about half as high as the Assam figures. Investigation of this subject in Assam has shown that a certain number of pregnancy anæmias is caused by iron deficiency from deficient iron intake and blood loss by hookworm infection, but that a balance of cases exists of macrocytic type the cause for which, apart from pregnancy, is not yet clear. Inquiry into the deaths from anæmia in Calcutta suggests that a number of them are caused by a deficient diet. In some of these cases there was a history of dysentery with consequent restriction of diet, which was continued for an unduly long period. Anæmia is also considered to be an important contributing factor in many of the deaths listed under other headings. This apparently serious cause of mortality among pregnant and parturient mothers has its bright side, for there are already indications that it can be largely overcome by appropriate treatment. Another not unsatisfactory aspect of the anæmia problem is that although it has been found necessary to add it to the international list of causes of maternal mortality on account of its frequency, if the deaths from this cause are deducted from the total it shows the figures for Calcutta in a much more favourable light in comparison with the maternal mortality rate in countries far ahead of India in their care of women during pregnancy, childbirth and the puerperium.

This report does not stop at a discussion of the causes of maternal mortality but it goes on to consider in detail how they may be best overcome, and it also discusses the extent of the properly organized maternity services in Calcutta. There is a final short chapter of recommendations based on the evidence produced by the inquiry: this we do not comment upon as we have reproduced it in full in our abstract of the report given elsewhere.

It is indicated that this is only the first of a series of inquiries which may be carried out by the Indian Research Fund Association in other

centres, both in town and country, and if they are conducted with the same care and energy as the one under review, they should add much further valuable information on how to deal with this problem. But, as practically everyone who writes on health problems concerning the whole of India is forced to remark, India is a vast country with many different climates and peoples with varied habits and religious beliefs with consequent differences in its local health problems; therefore if the investigation of

maternal mortality throughout the country is to be left to the sole efforts of the Research Fund Association it will be many decades before even the preliminary surveys are completed. It is accordingly suggested that now that this excellent report has been published it might be taken as a model for independent inquiries elsewhere, which could be profitably conducted by various local authorities, and in this way acquisition of the necessary preliminary information would be greatly speeded up.

## Special Article

### SOCIAL ASPECTS OF TUBERCULOSIS

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#### Introduction

Koch's discovery of the tubercle bacillus revolutionized the time-honoured conceptions regarding phthisiogenesis, but it has brought in its train new problems difficult of solution. Though the problem of tuberculous infection is adequately solved, a satisfactory explanation of tuberculous disease is still wanting. Bacteriology is considered by many as inadequate to clear up completely the ætiological problems of phthisis. Why, for instance, when the vast majority of urban populations are infected with tubercle bacilli consequent on its ubiquitous distribution, do only a small percentage of those so infected suffer from the ravages of the disease? Why should the disease take an acute course in some, resembling the conflagration in a forest fire, while in others it is chronic and slow, like a smouldering charcoal fire? Why should the pathological changes be so varied in different individuals? Why should some members of a tuberculous family suffer from the disease while others enjoy a relative immunity? The existence of such apparent discrepancies is sufficient testimony to the fact that the discovery of the tubercle bacillus as the causative organism in tuberculosis has only touched the fringe of the problem of phthisiogenesis. Attention has therefore been diverted to accessory non-parasitic causes of phthisis, both endogenous and exogenous. In the latter group of causes comes the important social factor including environmental peculiarities and economic conditions, such as occupation, housing, nourishment, etc., and also the geographical *milieu*.

#### Social factor in ætiology

Even in cities which boast of ideal methods of sanitation the incidence of infection with tubercle bacilli, as judged by the tuberculin test, is as high as in others less fortunately endowed. It has been shown that 90 to 98 per cent of urban

populations in Europe are infected with tubercle bacilli by the time they reach the age of 24. By no means yet known to man is it possible to prevent civilized mankind from coming into contact with tubercle bacilli. It is no doubt true that during infancy the well-to-do are shielded from contact with tuberculosis, unless one of the family or servants is affected with the disease, but when they reach the school-going age they come into contact with the outside world and hence are as liable to infection as those in the poorer strata of the population. Hence infection with tubercle bacilli is only slightly influenced by social and economic conditions. More important than infection is the question of morbidity due to tuberculosis. It has been statistically established beyond any possibility of doubt that tuberculosis is pre-eminently the poor man's disease. How does poverty increase the incidence of tuberculosis? This problem has to be looked at from various aspects. First and foremost is the question of malnutrition due to inability to buy the proper quantity, as well as quality, of foodstuffs. Stallybrass in 1931 says, whether it is through better nutrition or better housing or both it appears clear that if wisely expended and not wasted on alcohol, etc., rising wages produce a fall in tuberculosis. When therefore the incidence of tuberculosis morbidity is inversely proportionate to the wage-earning capacity its proportion among the unemployed will naturally be enormously greater. The tuberculosis mortality per 100,000 of population in the various parts of the city of Paris calculated by Bertillon is as follows:—

Age in years	..	1-19	20-39	40-59	Over 60
Very rich	..	61	129	159	105
Rich	..	79	205	241	168
Poor	..	168	526	641	340
Very poor	..	180	685	907	524

These figures are self-explanatory.

Apart from the question of malnutrition consequent on poor economic conditions, congestion of population is another equally important factor. It is a well-known fact that the incidence of tuberculosis is greatest in the slum areas



of every city where the poor live huddled together in insanitary and ill-ventilated dwellings. Besides poverty, overcrowding and filth may act by favouring contact infection.

In the city of Vizagapatam, where the writer has been working as Tuberculosis Officer for some years, the poor people live huddled together in huts of a peculiar picturesque construction. The average hut is built on a floor which is but 6 inches above the surrounding ground. The wall (there is only one wall as the structure is circular near the floor and tapers to a point at the top of the roof) is only 3 feet high made of bamboo poles and *tatties*. The roof descends from a central pole all over the wall giving the appearance of an occluded Buddhistic *stupa*. In each such thatched abomination live 5 to 8 people. Is it any wonder that the inhabitants of many of these groups of insanitary and ill-ventilated huts are infected with tuberculosis?

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Another contributing social factor is the fairly rapid urbanization and industrialization which are taking place in India, without the sanitary conscience of the nation being fully developed. This naturally leads to increasing incidence of tuberculous disease. Nor are the rural areas in India free from the ravages of the disease. This is due to people in the villages in the neighbourhood of a town seeking employment during the day in the city and going back for the night to their homes. The result is that they carry infection from the town to the villages which have no modern sanitation.

In all the big cities of the world, owing to the growth of travelling that is entailed in getting daily to and from work, the lack of facilities for recreation in the open air and the sense of irritation and anxiety which is so frequently associated nowadays with vocations followed and circumstances encountered in such places, there is lowering of resistance and consequent predisposition to tuberculosis.

One other social factor which contributes to the spread of infection and disease is the excessive crowding of people during fairs and festivals and the extensive movement of pilgrims which is a peculiar feature in India. It is estimated that about 20 million pilgrims travel every year from one end of the country to the other carrying in their train acute as well as chronic infectious diseases. The writer has had occasion to treat several of the pilgrims suffering from tuberculosis in his wards, on their return home after a pilgrimage to Benares where they not only attained merit but also acquired the disease.

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A close study of the rigorous campaigns instituted in many civilized countries towards prevention of tuberculosis reveals that far from their succeeding in their misdirected though well-meant efforts, they have only created an intense phthisiophobia. Fishburg considers it 'a vain effort to let loose swooping social service workers, like so many prohibition agents on defenceless tuberculous patients, and not a few who never had tuberculous disease. Follow them up, push them from pillar to post, interfere with their employment, with contracting suitable marriage, etc., as has been done in many cases with a view to preventing infection of fellow

centres, both in town and country, and if they are conducted with the same care and energy as the one under review, they should add much further valuable information on how to deal with this problem. But, as practically everyone who writes on health problems concerning the whole of India is forced to remark, India is a vast country with many different climates and peoples with varied habits and religious beliefs with consequent differences in its local health problems; therefore if the investigation of

maternal mortality throughout the country is to be left to the sole efforts of the Research Fund Association it will be many decades before even the preliminary surveys are completed. It is accordingly suggested that now that this excellent report has been published it might be taken as a model for independent inquiries elsewhere, which could be profitably conducted by various local authorities, and in this way acquisition of the necessary preliminary information would be greatly speeded up.

## Special Article

### SOCIAL ASPECTS OF TUBERCULOSIS

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#### Introduction

KOCH'S discovery of the tubercle bacillus revolutionized the time-honoured conceptions regarding phthisiogenesis, but it has brought in its train new problems difficult of solution. Though the problem of tuberculous infection is adequately solved, a satisfactory explanation of tuberculous disease is still wanting. Bacteriology is considered by many as inadequate to clear up completely the ætiological problems of phthisis. Why, for instance, when the vast majority of urban populations are infected with tubercle bacilli consequent on its ubiquitous distribution, do only a small percentage of those so infected suffer from the ravages of the disease? Why should the disease take an acute course in some, resembling the conflagration in a forest fire, while in others it is chronic and slow, like a smouldering charcoal fire? Why should the pathological changes be so varied in different individuals? Why should some members of a tuberculous family suffer from the disease while others enjoy a relative immunity? The existence of such apparent discrepancies is sufficient testimony to the fact that the discovery of the tubercle bacillus as the causative organism in tuberculosis has only touched the fringe of the problem of phthisiogenesis. Attention has therefore been diverted to accessory non-parasitic causes of phthisis, both endogenous and exogenous. In the latter group of causes comes the important social factor including environmental peculiarities and economic conditions, such as occupation, housing, nourishment, etc., and also the geographical *milieu*.

#### Social factor in ætiology

Even in cities which boast of ideal methods of sanitation the incidence of infection with tubercle bacilli, as judged by the tuberculin test, is as high as in others less fortunately endowed. It has been shown that 90 to 98 per cent of urban

populations in Europe are infected with tubercle bacilli by the time they reach the age of 24. By no means yet known to man is it possible to prevent civilized mankind from coming into contact with tubercle bacilli. It is no doubt true that during infancy the well-to-do are shielded from contact with tuberculosis, unless one of the family or servants is affected with the disease, but when they reach the school-going age they come into contact with the outside world and hence are as liable to infection as those in the poorer strata of the population. Hence infection with tubercle bacilli is only slightly influenced by social and economic conditions. More important than infection is the question of morbidity due to tuberculosis. It has been statistically established beyond any possibility of doubt that tuberculosis is pre-eminently the poor man's disease. How does poverty increase the incidence of tuberculosis? This problem has to be looked at from various aspects. First and foremost is the question of malnutrition due to inability to buy the proper quantity, as well as quality, of foodstuffs. Stallybrass in 1931 says, whether it is through better nutrition or better housing or both it appears clear that if wisely expended and not wasted on alcohol, etc., rising wages produce a fall in tuberculosis. When therefore the incidence of tuberculosis morbidity is inversely proportionate to the wage-earning capacity its proportion among the unemployed will naturally be enormously greater. The tuberculosis mortality per 100,000 of population in the various parts of the city of Paris calculated by Bertillon is as follows :—

Age in years	..	1-19	20-39	40-59	Over 60
Very rich	..	61	129	159	105
Rich	..	79	205	241	168
Poor	..	168	526	641	340
Very poor	..	180	685	907	524

These figures are self-explanatory.

Apart from the question of malnutrition consequent on poor economic conditions, congestion of population is another equally important factor. It is a well-known fact that the incidence of tuberculosis is greatest in the slum areas

of every city where the poor live huddled together in insanitary and ill-ventilated dwellings. Besides poverty, overcrowding and filth may act by favouring contact infection.

In the city of Vizagapatam, where the writer has been working as Tuberculosis Officer for some years, the poor people live huddled together in huts of a peculiar picturesque construction. The average hut is built on a floor which is but 6 inches above the surrounding ground. The wall (there is only one wall as the structure is circular near the floor and tapers to a point at the top of the roof) is only 3 feet high made of bamboo poles and *tatties*. The roof descends from a central pole all over the wall giving the appearance of an occluded Buddhistic *stupa*. In each such thatched abomination live 5 to 8 people. Is it any wonder that the inhabitants of many of these groups of insanitary and ill-ventilated huts are infected with tuberculosis?

One other important socio-environmental factor which favours the development of the disease is the attitude of the mind. In tuberculosis, more than in any other disease, the mental factor, such as domestic worry and unhappy surroundings, is an important contributing cause to the onset of the disease. The joy of life not only emanates from within but also from happy environmental circumstances.

The writer had the opportunity to treat one of the princes of India who lived in an atmosphere of suspicion and distrust consequent on domestic infelicity, before he fell a victim to tuberculosis. Mental worry in that case was certainly a potent predisposing factor in the development of the disease. The writer has also known of three nurses who developed tuberculosis a few months after being disappointed in love. On systematically enquiring into the life and environment of 100 consecutive patients prior to the onset of the disease it was found that 75 per cent of them gave definite history of serious mental worry. Whatever be the nature of worry, be it a disappointment in love or unhappy married life, or sudden and serious financial loss, an unhappy state of mind is certain to undermine the health of an individual and make him more susceptible to tuberculous infection. Among mental patients the incidence of tuberculosis is great in those who suffer from the depressive type of mental aberration.

Another contributing social factor is the fairly rapid urbanization and industrialization which are taking place in India, without the sanitary conscience of the nation being fully developed. This naturally leads to increasing incidence of tuberculous disease. Nor are the rural areas in India free from the ravages of the disease. This is due to people in the villages in the neighbourhood of a town seeking employment during the day in the city and going back for the night to their homes. The result is that they carry infection from the town to the villages which have no modern sanitation.

In all the big cities of the world, owing to the growth of travelling that is entailed in getting daily to and from work, the lack of facilities for recreation in the open air and the sense of irritation and anxiety which is so frequently associated nowadays with vocations followed and circumstances encountered in such places, there is lowering of resistance and consequent predisposition to tuberculosis.

One other social factor which contributes to the spread of infection and disease is the excessive crowding of people during fairs and festivals and the extensive movement of pilgrims which is a peculiar feature in India. It is estimated that about 20 million pilgrims travel every year from one end of the country to the other carrying in their train acute as well as chronic infectious diseases. The writer has had occasion to treat several of the pilgrims suffering from tuberculosis in his wards, on their return home after a pilgrimage to Benares where they not only attained merit but also acquired the disease.

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A close study of the rigorous campaigns instituted in many civilized countries towards prevention of tuberculosis reveals that far from their succeeding in their misdirected though well-meant efforts, they have only created an intense phthisiophobia. Fishburg considers it 'a vain effort to let loose swooping social service workers, like so many prohibition agents on defenceless tuberculous patients, and not a few who never had tuberculous disease. Follow them up, push them from pillar to post, interfere with their employment, with contracting suitable marriage, etc., as has been done in many cases with a view to preventing infection of fellow

workmen'. Again Baldwin as early as 1913 said 'Adults are very little endangered by close contact with open tuberculosis, and not at all in ordinary association. . . . It is time for a reaction against the extreme ideas of infection now prevailing. There has been too much read into the popular literature by health boards and lectures that has no sound basis in facts and it needs to be dropped out and revised'.

Anti-tuberculosis campaigns with glaring posters and popular lectures have certainly produced an unnecessary scare in the minds of the lay public who naturally begin to shun the unfortunate people who are afflicted or suspected of being afflicted with phthisis. This phthisiophobia is itself an indirect danger as is so clearly expressed by the American historian Garret Brown. 'Known and recognized and decently entreated, we are not dangerous. Victims ourselves of this same regime of ignorant and self-deceiving inhumanity we are called on every hour of our lives for a magnanimous consideration of others. Society can hardly find it surprising or a grievance if our human nature should sometimes weaken under the strain of the incessant provocation it endures from this strange working of human nature in general. . . . If the public is to be safe from us, if the public is to continue to have our protection from that against which it failed to protect us, then the public must make it possible for us to get what we must have to live. We are neither criminals nor mendicants. We do not ask favours, we merely revolt against a mean and stupid oppression. We revolt against ignorance and against a lie. The public would get rid of us, and thereby make us inescapable. It would pretend, and would have us pretend, that we are nowhere. It thereby ensured that we shall be everywhere. It proscribes us and thereby admits us'.

These methods of phthisiophobia ought to be avoided as they are not only unnecessary but positively dangerous. The patients are to be told that they are a menace only to infants and not at all dangerous to adults. They are sufficiently philanthropic to take proper precautions against infecting those who may be harmed by it. On the other hand, if these unfortunate victims of phthisis are goaded to desperation by subjecting them to unwarranted social ostracism and obloquy for no fault of their own, the problem of control will be rendered all the more difficult. Hence, it is the opinion of the writer that no kind of social disability or stigma should exist with respect to tuberculosis, as otherwise many of the patients will be driven underground and live in promiscuity, in which state they will be a potential danger as they will not be actuated by 'magnanimous consideration for others'. From the therapeutic point of view also, social disabilities of the tuberculous should be wiped out as the inferiority complex engendered thereby will have a depressive effect on the minds of the patients.

### *Social aspect of treatment*

If the community can demand of the consumptive to shape his life in such a manner as to prevent the dissemination of the disease, the consumptive has in his turn every justification to expect the community to be mindful of its own duties towards him, who is suffering to a great extent because of conditions which the authorities have permitted to prevail. They should not only see that conditions favouring development of phthisis should be eliminated but also provide shelter, proper nourishment and medical attendance for those patients who are not in a position to procure it at their own expense. It is the duty of the state to maintain an adequate number of tuberculosis clinics and provide accommodation for patients in hospitals and sanatoria. The conditions in India are indeed appalling. With a population of 370 millions out of which a moderately estimated 5 million are suffering from tuberculosis there are only 2,703 beds available in hospitals and sanatoria for the whole of India. It will not be out of place to remark, however, that the appeal for funds for an Anti-Tuberculosis Campaign made recently by Lady Linlithgow is extremely opportune and it is hoped that something tangible and substantial will be done in the near future to bring this disease under control in India.

Social and environmental conditions have an extremely important bearing on the treatment of tuberculosis. Experience as well as a general impression testify that in good social circumstances and in good living conditions tuberculosis takes a more favourable course than in a socially inferior environment. A patient who can afford to detach himself from his family and get treated for the proper period of time in an efficient institution, and subsequently to live the carefully regulated life prescribed under satisfactory conditions, with a good prospect of the benefit he has received from sanatorium treatment being consolidated, has a much better expectation of life than the one who is less fortunate in his social and economic level.

But there is one other aspect of environment which has not been adequately stressed. It has been found that too often men and women contract the disease even though their standard of living is high, their housing hygienic and their working conditions excellent. 'Not merely good material conditions, not merely physical exercise whether organized or otherwise, but a mental state . . . ' says Varrier-Jones. He also adds 'this mental state is of the utmost importance. It is produced by an imbalance of our endocrine system, and that imbalance somehow upsets and undermines resistance to disease'. In the actual treatment of the tuberculous patients the environment must have something psychological about it. There must be an atmosphere of encouragement. An attitude of hope and not despair, a quiet contentment engendered by

confidence in himself and those who look after him, and an optimistic cheerfulness will go a long way towards the arrest of the disease process. Material conditions alone cannot produce this result. The mind must be at ease too. The consequence of mental ease is certainly the restoration of endocrine balance. In the degree in which we can create the conditions for well being, in that same degree can we maintain our re-created resistance to disease.

When a small wage-earner, who is also the sole support of his family, falls a victim to tuberculosis, the source of income is suddenly stopped, unless his employer gives him leave for the sick period with full pay. This is extremely unlikely as it would be a financial loss to the employer who will have to pay not only the man on leave but also the man who is temporarily employed in his place. If it is only a question of a few weeks, it could possibly be adjusted. But the treatment of tuberculosis is a question of months and sometimes years. The state should therefore provide for free treatment for such individuals and for the support of their families during the period of their illness. Unless this is done the patients will not submit themselves for proper and prolonged treatment in state institutions, as they will naturally be anxious to get discharged as soon as they feel slightly better and go back to their work, as the life of their families depends on their working and earning. Even if they are compelled to stay in the hospital or sanatoria, their condition may not improve as their minds will always be in an anxious state with worry for their wives and children. Under both these considerations therefore the State should provide not only for the free treatment of the poor wage-earning consumptives but also for the adequate support of their families if they have no other source of income. The only other way by which the problem is to be solved is by insisting on an universal system of national health insurance by which the insurance companies are made to pay for the treatment of the insured person and also for the support of his family.\*

#### *Social aspect of after-care and rehabilitation*

The sanatorium form of treatment has come to stay. Collapse therapy and other therapeutic measures, in spite of the marvellous results produced, cannot replace institutional treatment but form an important and necessary ancillary to it. It was found, however, that though the immediate results of sanatorium treatment were promising, the follow-up statistics of Bardswell, Weickert and Brown showed the ultimate results

to be unsatisfactory. This was found to be due to the inability on the part of many of the patients to continue the same kind of regime for the prescribed period of time after discharge from the sanatorium. The after-care movement therefore is the logical outcome of sanatorium treatment.

The problem of rehabilitation can be considered from two aspects, firstly from that of the patient and his family and secondly from the point of view of social hygiene and prophylaxis by institutional segregation of the chronically sick.

The plea for an elaborate system of after-care from the point of view of the patients is itself a confession of our inability to effect complete cure in tuberculosis. The utmost one can hope for is the arrest of the disease process. The maintenance of the arrest necessitates, always a temporary and often a permanent, continuity of the regime of life prescribed and followed during the stay in the institution. Many of the return cases met with in sanatoria and hospitals are because of the sudden return to the old mode of life and environment immediately after discharge. This can in a good measure be avoided and the number of patients who can take their place in the open labour market can be considerably raised by means of long treatment supplemented by after-care.

According to Vos the after-care patients can be divided into three groups, namely, (a) those who after treatment varying in length are completely healed, (b) those who regain their full earning capacity through temporary after-care or those who retain it through permanent after-care and (c) those who cannot regain their earning capacity because their illness takes an inevitable and unstable course.

The creation of combined institutional and semi-institutional systems of treatment and after-care necessitates grouping together of different establishments which facilitates the easy passage of various grades of patients without discontinuity through the phases of convalescence (medical and social). This may be accomplished either by creating a series of separate institutions for each of the various phases connected with one another through a central organization or by building up multiple units, the various departments of which are adapted to the various stages of convalescence.

In most of the institutions intended for treatment and rehabilitation of tuberculous patients there is a threefold organization. The parts of the unit are :—

- (1) The sanatorium-hospital for treatment.
- (2) The after-care section as intermediary between clinical treatment and re-employment in normal or sheltered industries.
- (3) The village settlement with industries for sheltered employment.

\* [Note.—So far as the Editor is aware no country has hitherto provided for an universal national health insurance of its inhabitants. National Health Insurance Acts provide for wage-earners up to a certain level. Insurance companies insure for sickness and invalidity on payment of a premium. As such it cannot be a compulsory and universal procedure.—EDITOR, I. M. G.]



Economic and sociological laws govern the growth and determine the character of any rehabilitation scheme which also organizes the post-sanatorium life of the tuberculous.

A pertinent question that may be asked is whether such an elaborate system of after-care is warranted. The excellent results shown at the Papworth settlement are sufficient to justify the institution of after-care schemes. Even those who can be considered as completely arrested cases require prolonged convalescence in sheltered employment before they are allowed to go back to their old work and environment. There are others in whom the disease is stabilized but who are unfit to return to their previous employment but who are fit enough for working in other fields. These can easily be trained for their new jobs during their period of convalescence, living under a system of temporary sheltered employment. There are yet other sub-standard consumptives who can work only under constant supervision and who therefore have to live under a system of permanent sheltered employment. The remainder are chronic invalids who are permanently disabled and have to be segregated in these settlements.

The after-care schemes are directed towards the socio-therapeutic protection of the various

grades of ex-patients after their discharge from hospitals and sanatoria.

It may be asked why should the state concern itself with tuberculosis and the fate of tuberculous patients? It is because the state demands notification of the disease, to protect itself. But in protecting itself in this way it may be putting in peril the livelihood and the whole social status of the patient. His work and his home are liable to be prejudiced by notification. If the state demands protection at such a cost, it must accept the liability of providing sufficient compensation. The state should not only provide treatment but also see that the victim of the disease, if he cannot be cured, can be at least provided with employment in a suitable environment. The result of such efforts on the part of the state is threefold. The state is protected from infection; the patient's family also is similarly protected and finally 'a load of hopeless frustration is lifted from the shoulders of the patient himself'.

As tuberculosis is essentially a social disease, socio-economic considerations are of paramount importance in all the aspects of the tuberculosis problem. As with prevention so with after-care the problem of lessening the ravages of tuberculosis is again and again the problem of providing healthy conditions of living and working.

### BRITISH PHARMACEUTICAL PRODUCTS\*

TABLE I

*Showing foreign products of which there are British products with the same essential composition*

Foreign product	British product	British maker and/or supplier
Acecoline	Acetylcholine chloride	B. D. H.; B. W.; Evans.
Acidol	Pragmoline	M. & B.
Acidol pepsin	Betaine hydrochloride	Boots; B. D. H.; Evans.
Adalin	Betaine hydrochloride and pepsin	Boots; B. D. H.; Evans; Richter.
	Carbromal B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.; Richter.
	Planadalin	M. & B.
Afenil	Calcium chloride and urea	B. D. H.; Evans.
Agurin	Theobromine and sodium acetate	Boots; B. D. H.; Evans; M. & B.; T. & H. S.; Whiffen.
Airol	Bismuth oxyiodogallate B. P. C.	Boots; B. D. H.; B. W.; Evans; M. & B.; T. & H. S.; Whiffen.
Aluoin	Diamorphine hydrochloride B. P.	Evans; J. F. M.; M. & B.; T. & H. S.
Anæsthesin	Benzocaine B. P.	A. & H.; Boots; B. D. H.; Evans.
Aphrodine	Yohimbine	B. D. H.; Evans; Johnsons.
Aristol	Thymol iodide B. P. C.	A. & H.; Boots; B. D. H.; Evans; G. Chem.; Howards; M. & B.; Whiffen.
Arrhenal	Disodium methylarsenate	B. D. H.; Evans.
Atebrin	Mepacrine hydrochloride †	I. C. I.; M. & B.
	Quinacrine	M. & B.
Atebrin musonate	Mepacrine methanesulphonate †	M. & B.
	Quinacrine soluble	M. & B.
Atocin	Cinchophen B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Atophan	Cinchophen B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
	Tophosan	Richter.
Atophan balsam	Ung. Agotan co.	Howards.
Atoxyl	Sodium arsanilate	Evans; M. & B.
	Soamin	B. W.
Avertin	Bromethol †	Boots; B. C.; B. D. H.; B. W.; I. C. I.
Bayer 205	Suramin †	B. D. H.
	Antrypol	B. D. H.

\* Reprinted from the *Pharmaceutical Specialities*, second edition, published by the Association of British Chemical Manufacturers.

† Name chosen for use in the *British Pharmacopœia*.



TABLE I—*contd.*

Product	British product	British maker and/or supplier
	Vitamin B <sub>1</sub>	A. & H.; B. C.; B. D. H.; B. W.; Evans; Glaxo; M. & B.; Richter; Roche.
	Berin	Glaxo.
	Thianin	Richter.
	Benerva	Roche.
hydro-	Benzamine hydrochloride B. P. C.	Boots; B. D. H.; B. W.; Evans.
	Vitamin B <sub>1</sub>	A. & H.; B. C.; B. D. H.; B. W.; Evans; Glaxo; M. & B.; Richter; Roche.
	Berin	Glaxo.
	Thianin	Richter.
	Benerva	Roche.
Antaemame	Inj. bismuth salicylate B. P.	A. & H.; Boots; B. D. H.; Evans.
Cantan	Benzamine	Boots; B. D. H.; B. W.; Evans.
	Ascorbic acid B. P. (Vitamin C)	A. & H.; Boots; B. C.; B. D. H.; B. W.; Evans; Glaxo; Roche.
	Celin	Glaxo.
	Planavit C	M. & B.
	Redoxin	Roche.
Cebion	Ascorbic acid B. P. (Vitamin C)	A. & H.; Boots; B. C.; B. D. H.; B. W.; Evans; Glaxo; Roche.
	Celin	Glaxo.
	Planavit C	M. & B.
	Redoxin	Roche.
Chinosol	Potassium hydroxy-quinoline sulphate B. P. C.	A. & H.; Boots; B. D. H.; Evans; J. F. M.; Pierson.
	Soloid hydroxy-quinoline sulphate.	B. W.
Chloretone	Chlorbutol B. P.	A. & H.; Boots; B. D. H.; Evans; M. & B.; Morson.
Creosotal	Creosote carbonate B. P. C.	Boots; B. D. H.; W. J. B.; Evans; M. & B.
Decholin tablets	Dehydrocholic acid	B. D. H.
Decholin ampoules	Sodium dehydrocholate	B. D. H.
	Suprachol	Richter.
Dermatol	Bismuth subgallate B. P. C.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.; Morson; T. & H. S.
Devegan	Acetarsol vaginal compound	Evans.
	Stovarsol vaginal compound	M. & B.
Digitaline	Digitalin granules	A. & H.; Boots; B. D. H.; Evans.
Nativelle	Digitoxin	Boots; J. F. M.
	Tabloid digitalin cryst	B. W.
Dionin	Ethylmorphine hydrochloride B. P. C.	A. & H.; Boots; B. D. H.; B. W.; Evans; J. F. M.; M. & B.; T. & H. S.
Doryl	Carbachol*	A. & H.; B. W.
Duotal	Guaiacol carbonate B. P. C.	A. & H.; B. D. H.; B. W.; W. J. B.; Evans; M. & B.
Esterol	Benzyl succinate B. P. C.	A. & H.; B. D. H.; W. J. B.; Evans; G. Chem.
Eugallol	Pyrogallol monoacetate	B. D. H.; Evans; Johnsons.
Eumydrin	Atropine methyl nitrate	B. D. H.; T. & H. S.; Whiffen.
Euphthalmine	Tabloid ophthalmic euphthalmine hydrochloride	B. W.
Euphyllin	Theophylline and ethylenediamine	Whiffen.
	Aminophyllin	A. & H.
	Cardophyllin	Whiffen.
Euquinine	Quinine ethyl carbonate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Evipan	Hexobarbitone*	Boots; B. C.; B. W.; I. C. I.; M. & B.
	Hexamastab	Boots.
	Cyclonal	M. & B.
Evipan sodium	Soluble hexobarbitone*	Boots; B. C.; B. W.; I. C. I.; M. & B.
	Hexamastab sodium	Boots.
	Cyclonal sodium	M. & B.
Exalgin	Methylacetanilide B. P. C.	A. & H.; Boots; B. D. H.; Evans.
Perronyl	Citrated ferrous chloride B. P.	A. & H.; B. D. H.; B. W.; Evans; Howards; Johnsons.
Fibrolysin	Inj. thiosinamine and sodium salicylate B. P. C.	Boots; B. D. H.; Evans.
Fouadin	Stibophen*	B. W.; Glaxo.
Fraisse's ferruginous ampoules.	F. N. S.	A. & H.
Germanin	Suramin*	B. D. H.
	Antrypol	B. D. H.
Helmitol	Formamol B. P. C.	A. & H.; B. D. H.; Evans; H. & W.
Hydronal	Collumina	Evans.
	Alocol	Wander.
Hydropyryn	Lithium acetylsalicylate B. P. C.	A. & H.; Boots; B. D. H.; Evans; Howards.

\* Name chosen for use in the British Pharmacopœia.

TABLE I—*contd.*

Foreign product	British product	British maker and/or supplier
Hypophysin	Pituitary extract B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo; P. & B.
Ichthyol	Glandutrin Ichthammol B. P.	Richter. A. & H.; Boots; B. C.; B. D. H.; Evans; J. F. M.; M. & B.
Iodeikon	Iodophthalein B. P. Stipolac	A. & H.; B. D. H.; Evans. B. W.
Iodipin	Opacol; Opacin Iodised oil B. P. Iodatol	M. & B. A. & H.; Evans. B. D. H.
Iod-Tetragnost	Neo-Hydriol Iodophthalein B. P. Stipolac	M. & B. A. & H.; B. D. H.; Evans. B. W.
Lenigallol	Opacol; Opacin	M. & B.
Lipiodol	Pyrogallol triacetate Iodised oil B. P. Neo-Hydriol	B. D. H.; Evans; Johnsons. A. & H.; Boots; B. D. H.; Evans. M. & B.
Lipolysin	Iodatol (iodised oil 40%)	B. D. H.
Luminal	Anobesc Phenobarbitone B. P.	P. & B. A. & H.; Boots; B. D. H.; Evans; J. F. M.; M. & B.; T. & H. S.
Luminal sodium	Gardenal Soluble phenobarbitone B. P.	M. & B. A. & H.; Boots; B. D. H.; Evans; J. F. M.; M. & B.; T. & H. S.
Lutren	Gardenal sodium Lutcostab Progesterin Glanduantin	M. & B. Boots. B. D. H. Richter.
Magnesium perhydrol	Magnesium peroxide	A. & H.; Boots; B. D. H.; Evans; G. Chem.; H. & W.; Laporte; M. & B.
Medinal	Magnozon Soluble barbitone B. P.	Richter. A. & H.; Boots; B. D. H.; Evans; J. F. M.; M. & B.; Richter; T. & H. S.
Merkozone	Tabloid soluble barbitone Hydrogen peroxide 12 vols.	B. W. A. & H.; Boots; B. D. H.; Evans; G. Chem.; Laporte; M. & B.
Mercoloid	Collosol mercury sulphide	B. C.
Meta-Sympatol	<i>m</i> -Oxyphenyl-ethanolmethylamine hydrochloride	Light.
Migrainin	Phenazone caffeine citrate	A. & H.; Boots; B. D. H.; Evans; M. & B.; T. & H. S.
Myosalvarsan	Sulpharsphenamine B. P. Sulphostab Kharsulphan M. A. B. Sulfarsenol	Boots; B. W.; Evans; M. & B. Boots. B. W. M. & B. M. P.
Naganol	Antrypol	B. D. H.
Neohydropyrin	Magnesium acetyl-salicylate	B. D. H.; Evans; Richter.
Neosalvarsan	Magsyn Neoarsphenamine B. P. Novarsan Novostab Neokharsivan N. A. B.	A. & H. A. & H.; Boots; B. W.; Evans; M. & B. A. & H. Boots. B. W. M. & B.
Neo-trépol	Inj. bismuth B. P. Bismostab Hypoloid bismuth metal Bisglucol	A. & H.; Boots; B. D. H.; Evans; M. & B. Boots. B. W. M. & B.
Novocain	Procaine hydrochloride B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.; J. F. M.; T. & H. S.
Orthoform	Kerocain Planocaine	Kerfoot. M. & B.
Panflavin tablets	Orthocaine B. P. Planacrine	A. & H.; Boots; B. D. H.; Evans; M. & B. M. & B.
Pantopon	Papaveretum B. P. C. Alopon Opoidine Pavopin	B. D. H.; Evans; T. & H. S. A. & H. J. F. M. T. & H. S.
Parathormone	Parathyroid extract Euparatone	P. & B.; Richter. A. & H.
Pentnucleotide	Pentide S. P. N. Evans	A. & H. Evans.
Perhydrol	Hydrogen peroxide 100 vols.	A. & H.; Boots; B. D. H.; Evans; G. Chem.; Laporte; M. & B.

TABLE I—*contd.*

Foreign product	British product	British maker and/or supplier
Plasmoquine	Pamaquin *	I. C. I.; M. & B.
Preloban	Praequine	M. & B.
Progynon	Anterior pituitary extract	B. D. H.; Evans.
	Gonadotrophon	P. & B.
	Ovostab	Boots.
	Oestroform	B. D. H.
	Paboestrin	P. & B.
	Glandubolin	Richter.
Prolan	Physostab	Boots.
	Antostab	Boots.
	Gonan	B. D. H.
	Glanduantin	Richter.
Proluton	Luteostab	Boots.
	Progestin B. D. H.	B. D. H.
	Glanducorpin	Richter.
Prominal	Phemitone	I. C. I.
Prontosil Album	Sulphanilamide	A. & H.; Boots; B. C.; B. D. H.; B. W.; W. J. B.; Glaxo; M. & B.; M. C.; Morson; Richter.
	Streptocide	Evans.
Protargol	Silver protein B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Johnsons; J. F. M.; M. & B.; T. & H. S.
Pyoktanin violet	Methyl violet B. P. C.	A. & H.; Boots; B. D. H.; Evans; G. Chem.
Pyoktanin yellow	Auramine	B. D. H.
Pyramidon	Amidopyrine B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.; Richter, T. & H. S.
	Tabloid amidopyrine	B. W.
Pyramidon salicylate	Amidopyrine salicylate	A. & H.; B. D. H.; Evans; M. & B.; T. & H. S.
Salipyrin	Phenazone salicylate B. P. C.	A. & H.; B. D. H.; Evans.
Salit	Bornyl salicylate	B. D. H.; Evans; M. & B.
Salyrigan	Inj. mersalyl B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans.
	Hypoloid mersalyl	B. W.
Sanocrysin	Gold sodium thiosulphate B. P. C.	Johnsons; M. & B.
	Crisalbine	M. & B.
	Aurobin	Richter.
Sionon	Sorbitol	A. & H.; B. D. H.; Howards; M. & B.
Spirobismol	Quinine iodobismuthate	A. & H.; B. D. H.; Evans; Whiffen.
	Quinostab	Boots.
	Rubyl	M. & B.
	Bismosalvan	Richter.
Spirocid	Acetarsol B. P.	Evans.
	Orarsan	Boots.
	Kharophen	B. W.
	Stovarsol	M. & B.
Stypticin	Cotarnine chloride B. P. C.	A. & H.; Boots; B. D. H.; B. W.; Evans; J. F. M.; M. & B.; T. & H. S.
	Okistyptin	Richter.
Subitol	Ichthammol B. P.	A. & H.; Boots; B. C.; B. D. H.; Evans; J. F. M.; M. & B.
Superol	Potassium hydroxy-quinoline sulphate B. P. C.	A. & H.; Boots; B. D. H.; Evans; J. F. M.; M. & B.; Pierson.
	Soloid hydroxy-quinoline sulphate	B. W.
Suprarenin	Adrenaline B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; J. F. M.; M. & B.; P. & B.; Richter.
Sympatol	<i>p</i> -Oxyphenyl-ethanolmethylamine hydrochloride.	Light.
Synthalin B	Dodecamethylene diguanidine hydrochloride.	Light.
Tannigen	Acetanin B. P. C.	A. & H.; B. D. H.; Evans; H. & W.; M. & B.
Tannoform	Methylene ditannin	B. D. H.; Evans; M. & B.
Theocin sodium acetate.	Theophylline and sodium acetate B. P.	Boots; B. D. H.; Evans; M. & B.
Theominal	Tab. theobromine and pheno-barbitone.	A. & H.; Boots; B. D. H.; Evans.
	Tabloid Theoba	B. W.
	Theogardenal	M. & B.
	Theobromal	Richter.
Thiocol	Potassium guaiacol sulphonate B. P. C.	A. & H.; B. D. H.; W. J. B.; Evans.
Tiodine	Thiosinamine ethyl iodide	Boots; B. D. H.; Evans; Glaxo; M. & B.
	Iodolysin	A. & H.
Trional	Methylsulphonal B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; M. & B.; T. & H. S.

\* Name chosen for use in the British Pharmacopœia.

TABLE I—*concl'd.*

Foreign product	British product	British maker and/or supplier
Unden	Oestroform	B. D. H.
	Ovostab	Boots.
	Glandubolin	Richter.
Uroselectan B	Iodoxy* <sup>*</sup>	Glaxo; M. & B.
	Pyelectan	Glaxo.
	Uropac	M. & B.
Urotropin	Hexamine B. P.	A. & H.; Boots; B. D. H.; B'ton; B. W.; Evans; G. Chem.; Johnsons; J. F. M.; M. & B.; Richter.
Varicophytin	Hypertonic solution sodium chloride with anaesthetic.	B. D. H.; Evans.
Veronal	Barbitone B. P.	A. & H.; Boots; B. D. H.; Evans; J. F. M.; M. & B.; Richter; T. & H. S.
Veronal sodium	Soluble barbitone B. P.	Boots; B. D. H.; Evans; J. F. M.; M. & B.; Richter; T. & H. S.
Vigantol	Liq. calciferol B. P.	A. & H.; Boots; B. D. H.; Evans; Glaxo.
	Viosterol	A. & H.
	Radiostol solution and pellets	B. D. H.
	Tabloid calciferol	B. W.
	Ostelin	Glaxo.
	Devitol forte	Richter.
Xeroform	Bismuth tribromphenate B. P. C.	A. & H.; Boots; B. D. H.; Evans; Howards; M. & B.; Morson; T. & H. S.; Whiffen.
Yatren	Chiniofon B. P.	B. D. H.; Evans.
	Quinoxyl	B. W.
	Quinosulphan	M. & B.
Zinc perhydrol	Zinc peroxide	B. D. H.; Evans; G. Chem.; H. & W.; Laporte.

\* Name chosen for use in the British Pharmacopœia.

TABLE II

*Showing foreign products of which there are British products that have the same therapeutic properties*

Foreign product	British product	British maker and/or supplier
Albargin	Silver protein B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Johnsons; J. F. M.; M. & B.
Albucid	Sulphanilamide	A. & H.; Boots; B. C.; B. D. H.; B. W.; W. J. B.; Evans; Glaxo; M. & B.; M. C.; Morson.
	Streptocide	Evans.
	M. & B. 693	M. & B.
Algodorm	Barbitone and amidopyrin tablets B. P. C.	A. & H.; Boots; B. D. H.; Evans; Richter; T. & H. S.
	Allonal	Roche.
Antileprol	Ethyl hydnocarpate B. P.	S. A. S.; B. D. H.; Evans.
	Ethyl chaulmoograte	B. D. H.
	Moogrol; Iodised Moogrol; Alepol.	B. W.
Aperitol	Phenolphthalein B. P.	A. & H.; Boots; B. D. H.; Evans; G. Chem.; M. & B.; M. C.; Morson.
Arcanol	Acitophosan	Richter.
Aristochin	Quinine ethyl carbonate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Whiffen.
Arsen-tri-ferrin	Iron and arsenic injection ampoules and tablets.	A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo; Richter.
	Collosol iron and arsenic	B. C.
Aspiphenin	Tab. aspirin co. B. P. C.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
Asthmolysin	Pituitary extract and adrenaline	A. & H.; Boots; B. D. H.; Evans.
	Pitalin	P. & B.
Atophanyl	Cinchophen and sodium salicylate	Boots; B. D. H.; Evans.
	Tophosanyl	Richter.
Bioferol	Hepol with iron	A. & H.
	Livron	Boots.
	Crookes liver iron	B. C.
	Heprona; Hepatex with iron	Evans.
Bismarsen	Biarsamide; Bistovol	M. & B.
Cafaspin	Aspirin and caffeine	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards.
	Crookes anti-pyretic cachet	B. C.
	Kafalgol	Richter.
	Phensic	Veno.

TABLE II—*contd.*

Foreign product	British product	British maker and/or supplier
Calcimint	Calcium and vitamin D Calsolact Calsimil Salpern Kalsolac Ostocalcium	B. C. A. & H. B. D. H. Boots. Evans. Glaxo.
Calcium (Sandoz)	Calcium gluconate B. P.  Calcium laevulinate Percalcin Levu-Calcin (calcium laevulinate) ampoules.	A. & H.; Boots; B. D. H.; B. W.; Evans; G. Chem.; Howards; Kemball; M. & B. B. C.; B. W. Evans. Glaxo.
Campolon	Hepol; Ana-hepol; Azoule liver extract. Hepastab; Hepastab No. 2 Anahaemin; Liver extract (intramuscular injection). Neo-Hepatex Examen Parenamps Perhepar	A. & H.  Boots. B. D. H.  Evans. Glaxo. P. & B. Richter.
Carboserin	Activated carbon B. P. C.	A. & H.; Boots; B. D. H.; Evans; Richter.
Casbis	Injection bismuth B. P. Injection bismuth salicylate B. P. Stabismol Bisantol	A. & H.; B. D. H.; Evans. A. & H.; B. D. H.; Evans. Boots. M. & B.
Cignolin	Chrysarobin B. P.	A. & H.; Boots; B. C.; B. D. H.; B. W.; Evans; J. F. M.; M. & B.; T. & H. S.
Citobarium	Compound powder of barium sulphate B. P. C. Novumbrose; Umbrose Collosol barium sulphate Shadoform Barolac Fotonemal; Fotamealo; Fotamilko.	Boots; Glaxo.  A. & H. B. C. B. D. H. B. W. Evans.
Codeonal	Soluble barbitone and codeine	Boots; B. D. H.; Evans.
Compral	Tab. barbitone and amidopyrine B. P. C.	Boots; B. D. H.; B. W.; Evans; M. & B.
Cycloform	Benzocaine B. P.	A. & H.; Boots; B. D. H.; Evans.
Cycloform ointment	A B A ointment Benzocaine, extract of hamamelis and zinc oxide ointment. Ung. hamamelis co. Evans.	A. & H. B. D. H. Evans.
Cylotropin	Hexamine, sodium salicylate and caffeine. Saltetramine	B. D. H.; Evans. Richter.
Decicain	Cocaine hydrochloride	M. & B.
Dijodyl	Percaine hydrochloride Iodoprotein Iodicin Iodocasein	Ciba. Boots. B. W. Whiffen.
Eldoform	Albumin tannate	B. D. H.; Evans; M. & B.
Elityran	Thyroid B. P. Paromin	A. & H.; Boots; B. D. H.; B. W.; Evans; Richter. P. & B.
Ephetonin*	Ephedrine hydrochloride B. P.	A. & H.; Boots; B. C.; B. D. H.; B. W.; Evans; J. F. M.; M. & B.; Richter; T. & H. S.
Esmodil	Carbachol †	A. & H.; B. W.
Faexalin }	Yeast B. P. C.	A. & H.; Boots; B. D. H.; Evans.
Faexin }	Ergotoxine ethane-sulphonate B. P. (in obstetric practice).	B. D. H.; B. W.; Evans; M. & B.
Femergin	Sandalwood oil and Kava-kava resin.	B. D. H.; Evans.
Gonosan	Kavol	A. & H.
Gravitol	Ergotoxine ethane-sulphonate B. P.  Ernutin	A. & H.; Boots; B. D. H.; B. W.; Evans; Glaxo.  B. W.

\* Ephetonin, a racemic mixture, is made from synthetic ephedrine which has less therapeutic activity than the ephedrine (natural) shown as the British alternative.

† Name chosen for use in the British Pharmacopœia.

TABLE II—*contd.*

Foreign product	British product	British maker and/or supplier
Hegonon	Silver protein B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Johnsons; J. F. M.; M. & B.
Hepatopson liq.	Liquid extract of liver B. P. Hepol Hepatex; Neo-Hepatex Compound extract of liver Perhepar	A. & H.; Boots; B. D. H.; B. W.; Evans. A. & H. Evans. Boots. Richter.
Hexal	Hexamine B. P.	A. & H.; Boots; B. W.; B. D. H.; Evans; G. Chem.; J. F. M.; M. & B.
Hexophan	Cinchophen B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards; M. & B. Richter.
Hypertherman Icoral	Acetophosan Aolan Leptazol* (Penta-methylene- tetrazol).	Herts. Boots; Light.
Idozan	Phrenazol Dialysed iron Neo-ferrum Colliron	Boots. A. & H.; B. D. H.; B. W.; Evans; G. Chem. B. C. Evans.
Impletol	Procaine hydrochloride and caffeine.	B. D. H.
Inkretan	Thyroid and anterior pituitary Thyroxex co. Plurigland No. 3 Glandiposan forte	Boots; B. D. H. Evans. P. & B. Richter.
Juvenin	Yohimbine, nux vomica and damiana pills. Damiana co. pills	B. D. H.
Keraphen	Iodophthalein B. P. Stipolac	Evans. A. & H.; B. D. H.; Evans. B. W.
Krysolgan	Opaeol; Opacin Gold sodium thiosulphate B. P. C. Crisalbine; Myocrisin Aurobin	M. & B. Johnsons; M. & B. M. & B. Richter.
Lacarnol	Adenosine Carnacton Cardone	B. D. H. Cavendish. P. & B.
Lopion	Gold sodium thiosulphate B. P. C. Crisalbine; Myocrisin	Johnsons; M. & B. M. & B.
Mapharsen	Neosphenamine B. P. Novostab Neokharsivan	Boots; B. W.; Evans; M. & B. Boots. B. W.
Neo-Iodipin	Halarsol; N. A. B. Iodised oil B. P. Iodatol	M. & B. A. & H.; Evans. B. D. H.
Neo-Olesal	Neo-Hydriol Inj. bismuth salicylate B. P. Stabismol	M. & B. A. & H.; B. D. H.; Evans. Boots.
Neo-Reargon	Silver protein B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; Johnsons; J. F. M.; M. & B.
Neostibosan	Solid silver proteinate Neostam	B. W. B. W.
Neutralon	Magnesium trisilicate Colloidal kaolin Osmo-kaolin Lacto-kaolin Novasorb Alocol	A. & H.; Boots; B. D. H.; M. & B.; T. & H. S. B. D. H.; Evans. A. & H. B. C. Evans. Wander.
Noctal	Phenobarbitone B. P.	A. & H.; Boots; B. D. H.; Evans; J. F. M.; M. & B.; T. & H. S. M. & B.
Novalgin	Gardenal; Soneryl Somonal Amidopyrine B. P. Sonalgin Amidopyrine salicylate Saridone	Richter. A. & H.; Boots; B. D. H.; B. W.; Evans; T. & H. S. M. & B. B. D. H.; Evans. Roche.
Novasurol	Inj. mersalyl B. P. Hypoloid mersalyl Neptal	A. & H.; Boots; B. D. H.; Evans. B. W. M. & B.
Novatophan	Dilurgen Cinchophen B. P.	Richter.
	Acetophosan	A. & H.; Boots; B. D. H.; B. W.; Evans; Howards; M. & B. Richter.

\* Name chosen for use in the British Pharmacopœia.



TABLE II—*contd.*

Foreign product	British product	British maker and/or supplier
Novurit	Inj. mersalyl B. P. Hypoloid mersalyl Neptal Dilurgen Euflavine B. P. C.	A. & H.; Boots; B. D. H.; Evans. B. W. M. & B. Richter. A. & H.; Boots; B. D. H.; Evans; M. & B.
Panflavin Pantocain—see Decicain, p. 425. Pellidol	Scarlet red ointment B. P. C.	A. & H.; S. A. S.; Boots; B. D. H.; Evans; Johnsons; M. & B.
Petein Phanodorm	Whooping cough vaccine B. P. C. Allobarbitone B. P. C. Dial Soneryl Etoval Somnifaine Sulphanilamide	B. D. H.; B. W.; Evans; Glaxo. Boots; B. D. H.; Evans. Ciba. M. & B. Richter. Roche. A. & H.; Boots; B. D. H.; B. W.; W. J. B.; Glaxo; M. & B.; M. C.; Morson.
Prontosil rubrum	Streptocide Proceptasine; M. & B. 693 Soluseptasine Streptocide solution Antipyrin, phenacetin and caffeine Saridone	Evans. M. & B. M. & B. Evans. Boots; B. D. H.; Evans. Roche.
Quadronal	Antipyrin, phenacetin and barbi- tone.	B. D. H.; Evans.
Quadro-Nox	Ephedrine hydrochloride B. P.	A. & H.; Boots; B. C.; B. D. H.; B. W.; Evans; J. F. M.; M. & B.; Richter; T. & H. S.
Racedrin *	Iodoprotein Iodatol Iodicin Iodocasein	Boots. B. D. H. B. W. Whiffen.
Sajodin	Phenobarbitone B. P. Nembutal Gardenal	A. & H.; Boots; B. D. H.; Evans; J. F. M.; M. & B. Abbott. M. & B.
Seconal	Calcium gluconate B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; G. Chem.; Howards; Kemball; M. & B.; T. & H. S.
Selvoral	Calcium lactobionate Calcium laevulinate (laevulate) Percalcin Levu-calcin (calcium laevulinate) Silver protein B. P.	A. & H. B. C.; B. D. H.; B. W.; Evans; Richter. Evans. Glaxo.
Solargentum	Gold sodium thiosulphate B. P. C. Crisalbine Aurobin Myocrisin (aqueous) Myocrisin (oily) Procaine, strychnine sulphate and alcohol. Arecan spinal anæsthetic Duracaine (Procaine formula P. G.).	A. & H.; Boots; B. D. H.; B. W.; Evans; Johnsons; J. F. M.; M. & B.; T. & H. S. Johnsons; M. & B. M. & B. Richter. M. & B. M. & B. B. D. H.
Solganal B Solganal B Olcosum Spinocain	Arecan spinal anæsthetic Duracaine (Procaine formula P. G.).	Evans. M. & B.
Thiocol syrup	Bronchial syrup, Evans Novacol syrup Citro-Thiocol Thyroid B. P.	Evans. Richter. Roche.
Thyraden	Cresol B. P.	A. & H.; Boots; B. D. H.; B. W.; Evans; P. & B.; Richter.
Trikresol	Sulphanilamide	A. & H.; Boots; B. D. H.; Evans; G. S.; M. & B.; M. C.
Uleron	Streptocide M. & B. 693 Activated carbon B. P. C. Bornyl isovalerianate Menthyl valerianate Bornyl isovalerianate Hyoscine hydrobromide Hyoscyamine hydrobromide	A. & H.; Boots; B. C.; B. D. H.; B. W.; W. J. B.; Evans; Glaxo; M. & B.; M. C.; Morson. Evans. M. & B. A. & H.; Boots; B. D. H.; Evans; Richter. B. D. H.; Evans. A. & H.; B. D. H.; Evans; M. & B. B. D. H.; Evans. B. D. H. B. D. H.

\* Racedrin, a racemic mixture, is made from synthetic ephedrine which has less therapeutic activity than the ephedrine (natural) shown as the British alternative.

TABLE II—*concl'd.*

Foreign product	British product	British maker and/or supplier
Veramon	Barbitone and amidopyrin B. P. C. Sonalgin Veropyron Allonal	A. & H.; Boots; B. D. H.; Evans. M. & B. Richter. Roche.

## KEY

Abbott	= Abbott Laboratories, Ltd.	I. C. I.	= Imperial Chemical Industries, Ltd.
A. & H.	= Allen & Hanburys, Ltd.	Johnsons	= Johnson & Sons (Manufacturing Chemists), Ltd.
S. A. S.	= Stafford Allen & Sons, Ltd.	Kemball	= Kemball Bishop & Co., Ltd.
Boots	= Boots Pure Drug Co., Ltd.	Kerfoot	= T. Kerfoot & Co., Ltd.
B. C.	= British Colloids, Ltd.	Laporte	= B. Laporte, Ltd.
B. D. H.	= British Drug Houses, Ltd.	Light	= L. Light & Co., Ltd.
B'ton	= Brotherton & Co., Ltd.	J. F. M.	= J. F. Macfarlan & Co.
B. W.	= Burroughs, Wellcome & Co.	M. & B.	= May and Baker, Ltd.
W. J. B.	= W. J. Bush & Co., Ltd.	M. P.	= Modern Pharmaceuticals, Ltd.
Cavendish	= Cavendish Chemical Co.	M. C.	= Monsanto Chemicals, Ltd.
Ciba	= Ciba, Ltd.	Morson	= Thomas Morson & Son, Ltd.
Evans	= Evans Sons Lescher & Webb, Ltd.	P. & B.	= Paines & Byrne, Ltd.
Gen.	= Genatosan, Ltd.	Pierson	= Pierson Morrell & Co., Ltd.
G. Chem.	= General Chemical & Pharmaceutical Co., Ltd.	Richter	= Gedeon Richter (Great Britain), Ltd.
Glaxo	= Glaxo Laboratories, Ltd.	Roche	= Roche Products, Ltd.
G. S.	= Graesser Salicylates, Ltd.	T. & H. S.	= T. & H. Smith, Ltd.
Herts.	= Herts Pharmaceuticals Ltd. (formerly Beiersdorf Ltd.).	Veno	= Veno Drug Co., Ltd.
H. & W.	= Hopkin & Williams, Ltd.	Wander	= A. Wander, Ltd.
Howards	= Howards & Sons, Ltd.	Whiffen	= Whiffen & Sons, Ltd.

## ERRATUM

We regret that owing to an error 'Calsiod' on pages 176 and 179 of our March issue (wrongly spelt 'Calsoid' on p. 176) is listed as a foreign product. This is not the case, and we are informed that Messrs. Menley and James are the sole manufacturers of this product.

## Medical News

## MEDICO-SOCIAL QUESTIONS ARISING OUT OF THE MOVEMENTS OF CIVIL POPULATIONS

*Abstract report of the Emergency Sub-Committee of the Health Committee (League of Nations, Health Organization, Geneva, 4th to 7th March, 1940)*

AN attempt is made to state the principles and enumerate the measures which should be applied to control epidemic diseases and to protect the health of civil populations compelled, through hostilities or otherwise, to move from one area to another.

Displacement of a population may be compulsory or voluntary and, in addition, may concern only the native inhabitants of a given country or may include newcomers. The term therefore covers partial or complete evacuation of an indigenous population as well as the influx of refugees into a country from outside.

The following scheme is designed for a transfer of population under the most favourable conditions. Where speed is essential, however, whatever less elaborate action may be possible in the circumstances will obviously have to be accepted as sufficient.

The transfer of a population also raises a series of problems which are either purely social or have a bearing on economic policy or labour organization.

## I. MEASURES PRECEDING THE TRANSFER

The health authorities of the evacuated area and those of the reception area should make preliminary arrangements to facilitate co-ordination. Liaison should,

in particular, be established between the various medico-social services, especially those responsible for the reception, the isolation and the medical supervision of open cases of tuberculosis, other infectious cases and persons in need of special care.

The medical profession and the nurses and social workers should be familiarized beforehand with the work to be allocated to them. The social workers, for instance, will be responsible for explaining to the heads of families what rations, kit and other necessities are required and how these can best be carried.

In this connection, stress should be laid on the importance of the visiting nurses and social workers previously in charge of families of a locality population group remaining with that group both during the move and after arrival in the assigned reception area.

If it is necessary to spread the evacuated population over considerable areas, every effort should be made to regroup the families or even larger social units in order thus to reconstitute the transferred community as an entity with its administrative services.

Provision should be made for an order of priority in the execution of the plan, which should be determined by the existing circumstances, and should apply in particular to children and expectant mothers.

It is of importance that every person transferred should be provided with an identity document—i.e., identity discs (particularly for infants and children), individual or family evacuation booklets. Such a system is essential, not only in the interests of the individual, but also to apply all necessary supervision.

Preliminary propaganda and instructions should be undertaken among the population to be transferred as well as in the reception areas. This should include the education of women for the duties which will fall upon them. In this work, the co-operation of women's organizations may be extremely valuable. Teaching staffs can similarly play an important part—e.g., in preparing children for adaptation to life in a rural environment.

Propaganda in favour of voluntary evacuation may usefully be undertaken before compulsory evacuation becomes necessary.

The requisite measures are:

#### A. In the areas to be evacuated

Strict enforcement of existing or supplementary measures for the prevention of infectious disease and the protection of public health generally.

Propaganda by all available means (pamphlets, wireless, press, etc.) to promote vaccination against smallpox, diphtheria and the enteric fevers.

Registration, prophylactic medical examination and, when necessary, compulsory vaccination of persons to be evacuated.

Census of patients being treated in their homes.

Census of expectant mothers; classification according to the stage of pregnancy.

Ascertainment of open cases of tuberculosis, cases of venereal and other communicable diseases, 'carriers', cripples, mental cases, abnormal persons, etc.

#### B. In the transit areas

Provision of general and special means of transport (hospital trains, motor rail-cars and motor coaches fitted for stretcher cases, ambulances, etc.).

Provision of medical and nursing staff during the journey.

#### C. In the reception areas

##### 1. Choice of a reception area in relation to:

(a) Climatic conditions, local customs and the type of work of the transferred population.

(b) The health survey of the area.

Qualitative and quantitative survey of the water supply. Application of emergency methods of water purification.

General sanitation with particular reference to sewage and refuse disposal. Completion of any constructional work in hand and inauguration of essential supplementary schemes.

(c) The survey of available living accommodation.

Newcomers to a reception area may be billeted on the local inhabitants or housed in collective accommodation provided by existing buildings, reconditioned where necessary, or by hutments or camps. Due consideration should be given to the relative advantages and costs of each of these systems.

In the case of camps, important factors are the layout, internal equipment and the time required for erection.

In the accommodation survey, special provision for certain categories must not be overlooked—e.g., infants, children of school age, expectant and nursing mothers, old people, sick, cripples, mental cases and abnormal persons.

##### 2. Organization of reception.

Provision of:—Local services in charge of billeting; reception committees and headquarters; co-ordinating agencies between the various services; social centres and homes.

Arrangements should be made with a view to maintaining family and community life.

##### 3. Provision of medical and health services, including equipment.

(a) Arrangements for the maintenance in the reception area of the existing public health personnel and social workers and of an adequate number of doctors and nurses.

(b) Provision of adequate means of transport for doctors, nurses and midwives.

(c) Reinforcement of the hospitals and other institutions (maternity homes, hostels, crèches, milk dispensaries, etc.) either by enlargement of existing buildings or by the creation of new institutions in accordance with a general scheme of co-ordinated development.

Such a plan includes, in addition to general hospitals, sick bays for mild cases (infectious or non-infectious) and minor injuries, together with accommodation for unbillable children. Adequate provision is required of beds, drugs, dressings, sera and vaccines (including convalescent sera) as well as facilities for carrying out biological and bacteriological analyses.

The necessary preparations also include the provision of health centres, specialized dispensaries, infant welfare centres, bathing establishments, disinfection and disinfestation ovens, and their distribution according to a predetermined plan.

4. Survey of the available supply of food and milk and calculation of probable requirements.

5. Survey of available transport and estimated requirements.

#### II. MEDICO-SOCIAL WORK DURING THE TRANSFER

A. Assistance should be provided under medical supervision by nurses accompanying the population and by supplementary first-aid personnel.

B. Emergency hospital accommodation, canteens and milk kitchens, together with adequate sanitary conveniences (washing facilities and water-closets) should be provided at suitable points *en route*.

#### III. MEDICO-SOCIAL WORK IN THE RECEPTION AREAS

##### A. Medico-social supervision of evacuees

##### 1. Personnel:

Public health officers, medical practitioners, dental personnel, sanitary inspectors, midwives, nurses, health visitors, social workers, personnel of the Red Cross and first-aid organizations.

It is of fundamental importance that, as far as possible, the personnel should be that previously in charge of the transferred population. It is essential, for instance, that a social worker attached to a population group should accompany it during transit and remain with it in the reception area. It should, however, be supplemented, so far as may be necessary, by personnel recruited locally or requisitioned from another district.

Apart from its contribution to the general and social supervision of the population, the medical staff can in particular undertake prophylactic examinations (where these could not be carried out prior to departure), the detection and isolation of infectious cases, vaccinations, etc.

In every case, care should be taken to use, as far as possible, medical and social personnel who understand the language and habits of the transferred populations.

##### 2. Health centres and specialized dispensaries.

##### 3. Admission to hospital.

Adjustment of rules and financial conditions for admission.

##### 4. Mobile medical units.

General or specialized units (obstetrics, pediatrics, venereal disease, tuberculosis, dental care, laboratory examinations, etc.).

##### B. Hygiene of the reception area

Inspection by qualified personnel of the living accommodation provided.

Improvement of the prevailing sanitary standards of the billeting areas.

Periodic examination of drinking-water and supervision of sewage and household waste disposal, including fly, mosquito and rat control.

Maintenance of an adequate diet (collective feeding, school canteens, etc.).

Control of the purity of foodstuffs.

### C. *Special problems*

Enuresis and its prevention by education.

Pediculosis and scabies.

Psychological problems, including measures to counteract the ill-effects of the sudden change of environment.

### D. *Importance of general education in hygiene amongst the transferred population*

The measure of success achieved in the medico-social protection of the transferred populations will be to a great extent determined by the standard of public health organization already existing in the reception area.

In these circumstances, the raising of public health standards, and the strengthening of the medico-social machinery and equipment would appear to be the most logical and efficient method of preparing for the possible evacuation of populations and for their reception in other areas.

In this connection, general indications for guidance have been given by the Health Organization in the studies carried out in 1933 on the best methods of safeguarding the public health in times of emergency. Among these methods, one was particularly stressed—namely, the necessity for the thorough co-ordination of all the services and agencies, central and local, concerned. In view of the intricacy of the problems connected with extensive population movements, this recommendation is of particular importance. It is essential, therefore, that an endeavour should be made to secure agreement and unity of direction among the various ministries concerned and at the same time to enlist the active support of all public and private organizations (Red Cross societies, women's organizations, boy scouts, first-aid societies, etc.). Such co-ordination alone will yield the maximum of results with the minimum of expenditure.

### SCOPE FOR MANUFACTURE OF PAPAIN IN INDIA

THERE is ample scope in India for papain manufacture. With the world demand increasing and cultivation of the plant which yields it comparatively easy, and sites with requisite conditions of climate and soil numerous, the drug, at its present attractive price, offers promising possibilities for a large-scale industry in India.

### THE NAIR HOSPITAL DENTAL COLLEGE

#### *Announcement*

THE Nair Hospital Dental College is affiliated to the College of Physicians and Surgeons, Bombay, and is recognized to prepare students for L.D.S., C.P.S., Diploma Course.

Entrance requirement—Inter Science (B. group, same as medical students).

Course—Four years.

BOMBAY.

V. M. DESAI, D.D.S., F.I.C.D.,  
Dean.

### HILSA FISH IN THE RIVER HOOGHLY

#### *Extensive breeding grounds discovered*

STUDIES of the life-history of the *hilsa*, which is one of the most important edible fish found in Bengal, are being made by the Zoological Survey of India.

While carrying out biological investigations, at the Pulta Water Works on the river Hooghly, the Zoological Survey of India discovered fairly extensive breeding grounds of the *hilsa*, which is sometimes known as the Indian *shad*. Studies made since then indicate that the fish breeds in the Hooghly throughout the year, the peak period being July to August with a second low peak in May.

The upstream migration of *hilsa* on which the main fishery of this species depends, is believed to be due to the flooding of the rivers during the monsoon and the state of sexual maturity of the migrating individuals. Fluctuations are noticed in the year-to-year fishery, and it is surmised that a five-year cycle exists as in the case of the European herring.

### CINEOL CONTENT IN EUCALYPTUS OIL

#### *(Press communiqué)*

THE necessity of reducing cineol content in eucalyptus oil from 70 per cent as in the B. P. 1914 to 55 per cent, and introducing the change in the new edition of British Pharmacopœia to be published in 1941, has been suggested by the Indian Chemical Manufacturers' Association to the British Pharmacopœia Commission, London. The Association states that the examination of several samples of eucalyptus oil in India has shown that the cineol content is not more than 60 per cent and therefore the higher standard has been not only working as a severe handicap in the way of the development of the eucalyptus oil industry in India, but also precluding the manufacturers of pharmaceutical preparations in this country from using the Indian eucalyptus oil in the preparations of B. P. Products. It is pointed out that eucalyptus trees grow on a large scale in the Nilgiris and to a small extent in U. P., Bihar and other places in India and the Madras Government have expressed an opinion that if the cineol content is reduced to 55 per cent it would greatly benefit planters, distillers and merchants in the Nilgiris. The reduction of cineol content, it is stated, will greatly encourage the cultivation of eucalyptus and its utilization for oil which will enable India to produce considerable quantities of this oil and export it to foreign countries. As regards the effect of the change in the cineol content on medicinal value, the Association points out that Brevet-Colonel R. N. Chopra, Director, Biochemical Standardization Laboratory, Calcutta, is of the opinion that the reduction to 55 per cent would not be of great therapeutic significance. On the other hand Indian eucalyptus oil has several advantages over oils from other countries on account of its being free from obnoxious constituents.

## Special Report

### Health Bulletin No. 27. Abstract of the Report of an Inquiry into the Causes of Maternal Mortality in Calcutta

By M. I. NEAL EDWARDS, M.D., W.M.S.

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[In the introduction to this valuable report it is made clear that Calcutta was selected for this inquiry by the Maternal Mortality Advisory Committee of the

Indian Research Fund Association because of the facilities offered by the All-India Institute of Hygiene and Public Health and it does not mean that in the other cities (and the country districts) throughout India this subject is not of just as much importance. This is only the first of a series of such inquiries which it is the intention of the Research Fund Association to conduct as opportunity occurs, and no doubt other cities and rural centres will be selected for future inquiry.]

The object of this inquiry was to inquire into the number and investigate the causes of maternal deaths in Calcutta. The period during which follow-up of

deaths took place was 15th June, 1936, to 14th June, 1937.

The area chosen was that which is under the control of the Health Officer of the Calcutta Corporation.

The definition of 'maternal death' which has been adopted for the purpose of this inquiry was that used in the inquiry into maternal mortality made by the Department of Health for Scotland a few years ago and is expressed as follows:—

'Maternal deaths which occurred during pregnancy or within four weeks after the termination of pregnancy, or later if illness originated during pregnancy, childbirth or the puerperium.'

The registration cards in use provide no information regarding any relationship there may have been with pregnancy and childbirth, so cards were prepared identical with those in regular use by the sub-registrars but with the addition of the name of the inquiry and the following questions:—

Was she pregnant at the time of death?

Did she die during labour or abortion?

Did she die within three months after labour or abortion?

The health officer was kind enough to issue orders that these duplicate cards should be filled up for all female deaths between 10 and 50 years and that these cards should be returned with the ordinary registration cards.

We arranged to collect the duplicate cards daily from the health office and thereby obtained notice of deaths within one to three days of their occurrence so that investigation was possible with very little further delay.

Arrangements to receive the duplicate cards were made about three months before the inquiry actually started and cards were coming in regularly when the investigation of deaths began on 15th June.

It is impossible to say how accurately our findings represent the true maternal mortality in Calcutta during the year of the inquiry. The following are possible sources of error:—

1. Failure to register deaths.
2. Failure to receive duplicate registration cards in all cases.
3. Incorrect information obtained by sub-registrars regarding association with pregnancy or childbirth.
4. Failure on the part of sub-registrars to obtain information relating to pregnancy and childbirth.
5. Inability to trace cases of death in which the association with childbearing was definite or doubtful.

The omissions from amongst registered deaths which may have arisen in the ways suggested above are probably few.

A number of women come to Calcutta from rural districts and distant places for confinement and a proportion of these come on account of some complication of pregnancy or childbirth. Amongst the 887 deaths followed up there were 203 imported cases.

Two women doctors were appointed by the Indian Research Fund Association for the work of following up the deaths.

A weekly meeting between the investigators and the officer in charge of the inquiry was held for the purpose of reaching a conclusion regarding the cause of death and the avoidable factors present in all cases for which schedules had been completed within the previous week. In this way each case was discussed while the circumstances were fresh in the minds of the investigators and further details could be elicited or further inquiries made, if considered necessary.

The accurate estimation of the maternal mortality rate in Calcutta is not possible on account of defective birth registration and the fact that our series of maternal deaths unfortunately cannot be claimed to be complete.

The total number of registered live births which occurred during the period of the inquiry, from 15th June, 1936, to 14th June, 1937, was 28,714 and in addition 2,839 stillbirths were registered. The registration of stillbirths is believed to be even less accurate than

that of live births. It seems better therefore to express the rate per live births. The figures at our disposal, viz, 28,714 live births and 701 maternal deaths due directly to childbearing causes, give a maternal mortality rate of 24.41 per 1,000 registered live births. If imported cases are excluded the rate becomes 17.90 per 1,000 live births but the births in connection with some of the imported cases of maternal death were registered in Calcutta. The exact number of these births could not be estimated and excluded from the total registered births of the city. The rate of 17.9 must therefore be considered an under-estimate. The true maternal mortality rate in Calcutta remains unknown.

In classifying the cases according to the cause of death the *International List of Causes of Death* (1929 revision) has been followed as closely as possible. It has been found necessary, however, to make an additional heading for 'anæmia'. The relationship between the severe anæmias and pregnancy in India is probably an even more intimate one than exists between cardiac disease and pregnancy.

It was found that in the series of 887 maternal deaths there were 656 or 74 per cent of the total in which the registered and ascertained cause corresponded while in 231 or 26 per cent a different conclusion as to the cause of death was reached after investigation.

The 887 maternal deaths investigated have been divided into two classes:—

#### Cases

Class I.—Deaths due directly to childbearing 701

Class II.—Deaths due to an independent disease concurrent with pregnancy or childbirth .. .. 186

*Puerperal sepsis.*—In countries where registration of maternal deaths is carried out and where special maternal mortality surveys have been made, puerperal sepsis has been consistently found to be the most important cause of maternal death.

The small amount of evidence which is so far forthcoming in India, and all this evidence relates to urban conditions, goes to show that while the mortality rate in India is several times as high as in Western countries, the proportion of deaths from sepsis is not more than a third of the total and this in spite of the fact that a far larger number of deliveries in this country are attended by untrained women, who make no use of modern methods of asepsis and antisepsis.

*Anæmia.*—The inclusion of the anæmia deaths amongst 'childbearing' and not 'associated' causes needs further explanation. In the first place, whenever anæmia was clearly associated with other conditions such as kala-azar, epidemic dropsy, malaria, tuberculosis, the death has been assigned to the 'associated' group under the appropriate heading. Similarly all cases of anæmia in which other complications of childbirth were present have been assigned to their respective groups. Thus the sepsis, toxæmia, hæmorrhage and accidents of labour groups contain certain cases in which anæmia was probably the more important cause of death, the other condition being secondary or terminal. The anæmia cases which remained after exclusion of the above, have had to be classed with the limited information at our disposal, as due to anæmia *per se*.

Such evidence as we have collected in the course of this inquiry suggests that in Calcutta severe anæmias of both the macrocytic and microcytic type, and also mixed forms, are extremely common and that while many cases are associated with poverty and malnutrition, others occur amongst the well-to-do in families that seem healthy and well-nourished.

The association between a history of dysentery or diarrhoea and a severe pregnancy anæmia in the Calcutta series of cases was noticeable and the suggestion is put forward that the development of anæmia in these cases may often be the result not only of the intestinal infection but of the diet which is commonly prescribed in these cases, and often taken for long periods afterwards.

TABLE I  
Maternal deaths. Distribution by cause (International List, 1929 revision)

Deaths due directly to childbearing	Calcutta cases	Per cent	Imported cases	Per cent	Total	Per cent
Abortion (septic) .. ..	25	4.86	8	4.28	33	4.71
Abortion (non-septic) .. ..	2	0.30	2	1.07	4	0.57
Ectopic gestation .. ..	4	0.78	2	1.07	6	0.86
Other accidents of pregnancy ..	..	..	7	3.74	7	1.00
Hæmorrhage .. ..	65	12.65	9	4.81	74	10.56
Puerperal sepsis .. ..	172	33.46	52	27.81	224	31.95
Albuminuria and convulsions ..	75	14.59	51	27.27	126	17.97
Other toxæmias of pregnancy ..	11	2.14	4	2.14	15	2.14
Thrombosis and embolism ..	11	2.14	..	..	11	1.57
Accidents of labour and operative shock.	15	2.92	11	5.88	26	3.71
Other and unspecified puerperal conditions.	10	1.95	..	..	10	1.43
Anæmia .. ..	124	24.12	41	21.93	165	23.53
	514	100.00	187	100.00	701	100.00
Deaths due to associated diseases ..	170	..	16	..	186	..
TOTAL MATERNAL DEATHS ..	684	..	203	..	887	..

We have no evidence of how large a part hookworm infection plays in the causation of pregnancy anæmias in Calcutta.

**Eclampsia.**—Primigravida predominated and half the deaths from eclampsia occurred in women under 20 years of age. It was found that the women who died from eclampsia were relatively more from the middle class than the poor. Their diets were better, and fewer of them worked during pregnancy. It is the young newly-married woman in her first pregnancy, taking little exercise, living on a good diet, who seems more liable to develop toxæmia of pregnancy.

The most striking thing about this series of cases is the almost total lack of antenatal supervision which these women received and the failure on the part of the patients, doctors and relations alike to realize the serious nature of the warning symptoms which were present in a large proportion of cases and, in many, were of long standing.

**Hæmorrhage.**—Many of these deaths were undoubtedly preventable. The group includes some of the worst cases of mismanagement, delay in getting skilled assistance and failure to treat the blood loss, that were met with during the course of the inquiry. Warning hæmorrhages were present in half the cases of death from placenta prævia, but in no case were adequate steps taken to ensure safe delivery.

Amongst the deaths from postpartum hæmorrhage the number delivered by trained attendants was rather high which raises the question as to whether such attendants are inclined to try to hurry the third stage of labour.

**Abortion.**—All the women who died of septic abortion were either admitted to institutions or were seen by doctors at home and it is therefore highly probable that there were other deaths from abortion which we failed to discover during the year of inquiry.

**Accidents of labour.**—Deaths due to accidents of labour, i.e., due to the shock of labour itself, apart from hæmorrhage, made up a small proportion of maternal deaths in our series, and one is led to the conclusion that neglected cases of obstructed labour are rare in Calcutta.

**Tuberculosis.**—Tuberculosis was of outstanding importance in the 'associated' group and caused 41 per cent of all maternal deaths due to intercurrent diseases.

[Following this chapter there is a short one devoted to preventability, chapter 3 discusses the factors that were found to affect mortality and chapter 4 is a review of the hospitals and institutions where women can obtain help in childbearing as well as the organizations for home visiting and treatment. Unfortunately this chapter is headed 'The Military Services in Calcutta' which according to the index should read 'The Maternity Services in Calcutta'. Chapter 5 is given in *extenso*.]

#### CHAPTER 5.

##### *Recommendations suggested by the findings of the inquiry*

(1) **Vital statistics.**—Registration of births is very defective in Calcutta, more especially in some areas and amongst certain sections of the population. The possession of accurate information regarding the total number of births, live and still, is a basic requirement in drawing up adequate schemes for maternal care and it is therefore urged that steps be taken to enforce the Calcutta Midwives Act, 1923, Section 451 (which requires registration of births within eight days), if necessary by means of prosecutions for contravention of the law.

Information with regard to the age and parity of the mother, the place of delivery and the attendant at delivery, are additional facts which could be collected at the time of registration of births and if available would provide most valuable information for the further elucidation of facts relating to childbirth in the city. The possession of such information would greatly facilitate the registration and control of private midwifery practice, private maternity homes and the work of the untrained *dai*, and is a most desirable supporting measure for the Bengal Nurses and Midwives Act, 1934.

In the interest of greater accuracy in the registration of deaths, it is suggested that the primary and secondary causes of deaths should be stated on the death certificate and that the annual reports of deaths by cause should be prepared according to the International List of causes of death with an additional heading for anæmia in the childbirth group.

(2) **Organization.**—In the interest of better co-operation between the existing services, and of developing plans for future extension and improvements, it is



suggested that a co-ordinating body should be formed of representatives of (1) hospitals admitting maternity cases, (2) the department of the municipal public health service concerned with maternal care, (3) the voluntary organizations which are carrying on maternity work in Calcutta, (4) the anti-tuberculosis service and other allied services. It should be the function of such a body to obtain in the first place complete information regarding existing facilities and then armed with accurate knowledge of the total number of deliveries per annum in the city, to consider means of increasing the efficiency of the existing services and making plans for their future development.

The recommendations which follow make no pretence to completeness. They are outstanding points noted during the course of this inquiry and arising out of its findings and they are such as might be taken into consideration by a co-ordinating body, such as that suggested above, in the course of its deliberations.

(a) *Staff*.—Doctors and midwives employed by public health authorities and voluntary organizations for maternity work should have had special training in the preventive aspects of maternal care. The medical training of the sub-assistant surgeon is by no means an adequate preparation for work of this kind and the same is true of the course for training of midwives in many institutions. The fact that several hospitals which train medical students and midwives in Calcutta have neither antenatal nor post-natal clinics is sufficient evidence of the truth of this statement.

More use should be made of the health visitor in the existing maternity services, both for follow-up work in the homes and for the supervision of midwifery. The trained health visitor is the backbone of the welfare centre system and at present, adequately staffed welfare centres are confined to the scheme of work of voluntary organizations in Calcutta.

The work of midwives should be adequately supervised and refresher courses should be arranged. The number of cases which the midwife takes in a month should not be greater than she can properly attend to in that time. The number will depend to some extent on the area in which she works, but it should not exceed 15 cases a month.

(b) *Antenatal care*.—1. Systematic antenatal care should be provided in connection with all hospitals admitting maternity cases, maternity homes, welfare centres and domiciliary maternity schemes. This antenatal care should include consultation clinics held by a doctor and follow-up work in the homes.

2. The system of booking for confinement should be introduced in institutions admitting maternity cases and annual returns should be made for booked and emergency cases.

3. The extension of the intensive type of welfare centre work which includes systematic antenatal care (as at present carried on in small circumscribed areas in Calcutta by the welfare centres of the Indian Red Cross Society, and the Institute of Hygiene centre), so that all areas are covered, is recommended. The desirability of domiciliary midwifery being carried on in connection with such centres is emphasized. This makes for continuity of work, and direct supervision of the midwives by health visitors becomes possible.

4. Milk and extra nourishment should be available for pregnant women in poor circumstances, who are unable to obtain proper food, and should be distributed as part of welfare centre antenatal care.

5. In view of the importance of the complications of pregnancy, especially anaemia, the toxæmias and tuberculosis, the need for a generous supply of beds for antenatal cases in institutions is of the greatest importance in Calcutta. It is necessary not only that the number at present available should be greatly increased, but that closer co-operation should exist between welfare centres, domiciliary schemes and the hospitals so that those cases found to require institutional treatment in pregnancy may have the means of obtaining it.

(c) *Intranatal care*.—1. More beds for confinements both in hospital and maternity homes, especially for women of the Mahomedan community, who at present take relatively less advantage of the facilities offered, are greatly needed. In addition a sufficient number of beds must be provided for those whose homes are entirely unsuitable for confinement.

2. Regulations for the control and supervision of maternity homes should be introduced. The prevention of overcrowding, the provision of an adequate and trained staff and the proper segregation of infected or potentially infected cases are the outstanding requirements.

3. More provision is necessary for beds for cases of puerperal sepsis delivered at home. Such beds should be in a separate block if possible, or at least in a separate ward, and arrangements for the care of the infant while the mother is in hospital should be made.

4. When a case of puerperal sepsis occurs in the practice of a midwife she should not be allowed to attend normal confinements as long as she is in attendance on the septic case.

(d) *Postnatal care*.—Postnatal clinics (with arrangements for gynaecological treatment if necessary) should be held in maternity hospitals, maternity homes and welfare centres. Birth control advice should be available for those women for whom rapidly repeated pregnancy is undesirable on health grounds.

(c) *Special considerations*. 1. *Anæmia*.—The diagnosis and early treatment of anaemia in pregnancy is such a vital one in Calcutta that special methods of tackling it, apart from ordinary antenatal care, are needed. It is suggested that (1) all antenatal clinics should have access to a central laboratory where examination of blood of anæmic women can be carried out; (2) that certain hospitals should provide special wards for the treatment of anaemia in pregnancy and (3) that the necessary treatment for milder cases as out-patients should be available free of charge to poor patients at welfare centres, hospitals and maternity homes. The lay public, the health worker, midwives and doctors should be taught to recognize the early symptoms and signs of anaemia and to know what steps are necessary in order to get adequate treatment in pregnancy.

2. *Tuberculosis*.—The problem of the tuberculous mother, when home conditions are unfavourable, is one that can only be properly dealt with by providing institutional accommodation for her and segregation for the infant. Until such time as facilities for this are available, the provision of extra nourishment during pregnancy and lactation, and the closest possible co-operation between the maternity services and the anti-tuberculosis service are required in order to reduce the ravages of this disease. This problem is undoubtedly the most complex of those relating to maternal mortality in Calcutta, and raises difficulties which seem almost impossible of solution.

The recommendations given are indications of the serious deficiencies, in the management of pregnancy and childbirth in Calcutta, revealed in this report; part II which follows is devoted to a detailed discussion of the causes of death, brought out in this inquiry.]

## Current Topics

### A Programme for Early Aggressive Treatment of Pulmonary Tuberculosis

By C. F. HEGNER, M.D.

(From the *Journal of the American Medical Association*, Vol. CXII, 14th January, 1939, p. 136)

PULMONARY tuberculosis is a chronic systemic disease with a decided tendency to heal. The chronicity, inherent tendency to heal and curability are due to a

beneficent auto-immunization. Were this not true the human race would long since have vanished. This chronicity, when the disease is untreated, inadequately treated or unrecognized, is responsible for its continuous contagion and universal distribution, for a reducible economic waste and disability and for a certain irreducible mortality rate.

A programme for early aggressive treatment of pulmonary tuberculosis is properly initiated by the diagnosis of the disease in the earliest possible stage. During the period of inception and the early stage more can be accomplished by less therapy than at any time thereafter.

The inception of tuberculosis is subtle, the onset insidious and the early progress stealthy and so devoid of symptoms that the host is taken unawares.

When the disease first becomes clinically manifest it is usually not in the early stage but is well developed, with focal tissue changes more or less advanced.

The earliest general clinical symptoms due to altered physiology are not positive. They are largely inferential. The earliest local signs dependent on pathologic changes are positive. These are differential.

The preclinical and early clinical stages are often overlooked even by expert examiners. Errors in diagnosis are more frequently made by the less expert and those who are not tuberculosis minded. Physicians must become tuberculosis minded and appreciative of their fallibility. The usual methods of examination for early tuberculosis have definite diagnostic limitations.

However experienced, one cannot place complete reliance on one's skill in auscultation and percussion. Additional corroborative methods of examination must be used; the tuberculin test must be used with children and in all suggestive cases fluoroscopic examination must be done and roentgenograms of the chest made. To be dependable x-ray examinations must be interpreted by experienced physicians or experts in pathologic changes of the lungs as depicted by x-ray examination.

In borderline cases the x-ray examination cannot determine the grade of activity of a tuberculous lesion. It does portray more accurately than any other diagnostic procedure the presence and extent of lesions.

It is obligatory to check the physical signs with those shown by x-ray examination.

The success of the antituberculosis campaign has been brilliant. Much remains to be accomplished before the disease is vanquished. The incidence of and the deaths due to pulmonary tuberculosis have decreased roughly 60 per cent in the last twenty years. The 40 per cent ratio of deaths to the number of cases has not changed materially, notwithstanding the tremendous increase in hospitalization and sanatorium care and the advances made in the active treatment of the disease. The causes of this constant death ratio warrant critical analysis. The ratio is a challenge. An aggressive programme of case and feeder finding by which the disease can be diagnosed and treated at its very inception, and isolation or control of those who, wittingly or unwittingly, are disseminators of the disease, offer a most potent answer to this challenge.

The antituberculosis programme in the past has been of necessity largely one of defence against active phases of the disease. One waited until the victims were well seeded with tubercle bacilli or for their lesions to become definite before beginning active treatment.

To wait for the disease to become clinically manifest is to wait too long. Procrastination compounds difficulties, augments the uncertainty of therapy, prolongs disability, increases expense, spreads infection and multiplies mortality.

Prophylaxis is certain, while cure is uncertain when the disease is fully developed and impossible in a fairly fixed percentage of cases. These facts are established by the convincing investigations and mass studies for case finding and tracing all contacts to the source of infection. Though it is not always possible to trace the infection to its source, these surveys reemphasize the fact that every case of pulmonary tuberculosis originates directly or indirectly from some previous

case. The reports further prove that early pulmonary tuberculosis, especially in adolescence and early adult life, the periods during which, in the majority of cases, the disease first becomes active, is commonly symptomless and hence frequently undiagnosed.

One must face facts. The antituberculosis campaign of the future to be fully effective must be not only one of defence but also one of offence. An aggressive campaign of case and feeder finding would attack the disease before the tubercle bacilli became seeded, and active therapy would be begun months or years before irreparable damage to the tissues had time to develop. It is easier to prevent than it is to cure destruction of tissue and complications.

The early recognition and treatment of the infected and control of the infectors is logical, economical and practical. Patients with open tuberculosis must be isolated whenever possible. If sanatorium isolation is impossible, then the utmost should be done by a course of sanatorium treatment and instruction to control or render them innocuous. The contacts must be treated before they in turn have active open tuberculosis.

By such a programme the incidence and life history of tuberculosis will become known and its methods of spread understood. Both the profession and the public will become sensitized to the importance of competent periodic health examinations, to the necessity of early diagnosis and to the advantages of early treatment. Thus fortified, many of the present problems in treatment and most of the weak points in the fight against tuberculosis will be overcome.

Tuberculosis is recruited from the ranks of those who are in apparent health. It is no respecter of class, creed or colour and knows no geographic, political or social boundaries. A competent, efficient antituberculosis programme must be one of stern defence and aggressive offence, coextensive with the distribution of the disease.

#### NECESSITY OF EARLY CASE FINDING

A campaign of early case finding, national in scope, and the isolation or control of bacilli breeders and disease disseminators will accomplish more than any other, if not all other, factors in the treatment and eradication of pulmonary tuberculosis.

This is a large and expensive programme beyond the authority and means of private enterprise. One can participate in appointing qualified commissions to study, and in organizing competent agencies to carry on this important work. Co-operation of the public with the profession is essential to the success of any health programme. An enlightened public sentiment will support and later demand public health projects. Success in the control and elimination of one disease reacts favourably and forcefully on campaigns for the control of other diseases. A national health department is indispensable for the coordination of complex public health activities.

Conservation of public health and control of communicable diseases are the province of the federal government and its various subdivisions. They have the authority to make and enforce health regulations.

A national department of public health should promptly take up and vigorously extend nationwide compulsory mass surveys for case and feeder finding. Small groups of investigators within their limited means and scope have proved the importance and value of such surveys on a voluntary basis. The trail has been blazed, the administrative set-up pioneered and the feasibility of the plan assured.

The treatment of the ill is not the jurisdiction of governmental agencies. This has been, is and should continue to be the prerogative of private physicians. The confusing of federal, state and civic obligations with private and professional affairs begets irresponsibility, inefficiency and distrust. This truth is more certain in the realm of therapy than in any other field of endeavour. Regimentation of doctors is possible though highly undesirable. Regimentation of therapy worthy of respect is impossible.

The requisites for an efficient aggressive programme for the control and eradication of pulmonary tuberculosis are:

First in point of time and importance, an authoritative mass survey, national in scope, of case and feeder finding.

Second, continuous maintenance by the medical profession of a true appreciation of the character of the disease. It is expedient to consider tuberculosis more serious than the clinical symptoms indicate.

Third, early treatment. The earlier appropriate treatment is begun, the more consistently enforced by the physician and the more conscientiously followed by the patient, the more rapid and certain will resolution ensue.

#### EXPECTANT TREATMENT

The passive or expectant treatment of pulmonary tuberculosis is founded on the time-tried and proved principles of general rest, fresh air and wholesome food. To this honoured triad, modern active treatment has added collapse therapy to secure local rest to the diseased lung. The therapeutic result will be proportionate to the degree, duration and timeliness of general plus local rest. This is true not only in the early stages of the disease but also in advanced stages and in cases in which the disease is resistant and demands some form of surgical aid.

Every patient differs in his local and general reaction to infection. The dose and degree of virulence of the infecting organism and the grade of susceptibility, which fluctuate from time to time, determine the clinical symptoms, the character and intensity of the pathologic changes and the course of the disease. The response to therapy likewise varies. The pulmonary lesions are an accurate index of the trend of battle between the tubercle bacilli and the resistance of the patient. The evolution of the local lesions must be as closely followed as is the general progress made by the patient in order to estimate, round by round, his ability to overcome the disease. The course and severity of the clinical symptoms do not constantly parallel the pathologic changes in the tissues. This lag in constitutional reactions is deceptive.

No one can deny the importance and value of expectant treatment in early stages or that in many cases it fails, without additional aid, to control the progress of the disease.

#### COLLAPSE THERAPY

General rest and expectant treatment should be tried for a reasonable time, a period expressed in terms of weeks. As long as favourable progress is made, one should defer active therapeutic measures. When favourable progress is not made or ceases, active measures to secure the added benefits of local rest by some form of collapse therapy are promptly indicated. Collapse therapy is not a substitute for any of the older forms of treatment; it is an invaluable supplement to these when after a reasonable trial they have failed, or in the light of experience are destined to fail, to reestablish a resistance balance against the disease.

The earlier a focus not controlled by expectant treatment is attacked by the appropriate measure for collapse, the more certain, rapid and favourable will be the effect and the fewer the complications.

One must obtain promptly the minimum collapse of the lung that is conducive to healing all the tuberculous infiltration and cavitation. A more extensive procedure than is needed to control the lesion should be avoided. Unnecessary destruction of tissue and of functioning lung parenchyma will be prevented.

A variety of mechanical procedures have been devised to control different stages of the disease. They all have definite indications and limitations. There is an optimum time for each procedure, which if not taken advantage of leads to more extensive operations.

Every patient who presents indications for more radical procedures of surgical collapse is a living example of failure; a failure of the physician to diagnose early, to appreciate the gravity of the disease and to institute promptly and continue rigidly appropriate conservative measures, a failure of the patient to cooperate or of the disease to respond to the expectant

treatment, or a failure of the physician to resort early to less radical measures for collapse therapy. A favourable opportunity lost renders the general condition of the patient more serious and permits the development of complications or extension of the disease to irremediable stages.

Surgeons have learned the necessity of early operations in the treatment of cancer, the advantage of operating during the rising tide of reserve in thyrotoxic states and the diminished hazard in multiple stage operations in the case of properly prepared patients with prostatic disease. These lessons are equally applicable in the surgical treatment of pulmonary tuberculosis. Timely surgical intervention is truly conservative. Late operations are always of greater magnitude and danger, and the results are not so satisfactory as those of early operations.

The purpose of collapse therapy is to secure local rest to the diseased lung, to prevent the development of restraining mechanical factors and to eliminate impediments to contraction of the diseased area of the lung. The objective of compression therapy is actively to compress the cavity or the cavity-bearing area of the lung and control resistant interposed lesions which interfere with contraction and healing. The advantages of timely collapse therapy are proved by the splendid results attained with progressive and otherwise hopeless conditions. Delay in the diagnosis of pulmonary tuberculosis has been and is the chief obstacle to the control of pulmonary disease. Delay in instituting graded collapse therapy compromises and may defeat all efforts to cure.

Successful collapse therapy for pulmonary tuberculosis is not merely a matter of technique. Important as this is, of greater importance is the choice of procedure, the time and the degree of collapse needed. There is no procedure yet devised that is universally applicable to the fluctuating phases of the disease. Each procedure must be graded to control the local lesion. This involves an understanding of the patient, who is always a substandard surgical risk, a grasp of the mechanics of the thorax and the physiology of respiration, an estimate of the cardiac reserve and a knowledge of the pathology of all stages of the disease.

A surgeon should approach a case of pulmonary tuberculosis from a medical no less than from a surgical point of view. He should collaborate with the phthisiologist and the radiologist, who must become surgically minded. They must understand all phases of the disease and the indications and possibilities of combinations of the two plans of treatment.

Competent surgical treatment without continued intelligent general medical care cannot cure. Adequate timely surgical treatment can and does render local conditions favourable for the orderly processes of healing to effect an arrest or cure.

Pulmonary tuberculosis demands medical supervision from its inception until it is clinically cured. Too often this fact is overlooked in the treatment of patients subjected to surgical collapse. The patient and sometimes his physician are deluded by the immediate improvement secured by surgical intervention. They relax in the care which is vital to making that improvement permanent. For a lasting cure it is obligatory that the patient continue for months after operation a graded rest regimen. Adequate prolonged collapse facilitates the permanent obliteration of cavities and the healing of pericavitary lesions by fibrosis. No operation can do more.

Before operative intervention is decided on, a review of the history and a careful complete examination of the patient should be made; a meticulous study of the evolution and the present status of the lesions in the lung, so graphically and chronologically recorded by a series of x-ray films, is imperative. The information obtained is of inestimable value in deciding what, if any, surgical intervention is indicated.

Select that procedure which will be most effective for the given stage. When possible employ revocable measures in ascending grades of severity, giving each procedure a reasonable period to prove its capacity to control the lesion. Note the progress by repeated

physical examination and x-ray study. With contralateral lesions, and these are always present in some degree, the responsibility is augmented in proportion to the extent and grade of activity; one must proceed with caution, keeping well within the limits of respiratory and cardiac reserve.

When revocable measures are not indicated or have failed to control the progress of the disease, then irrevocable measures for selective compression are indicated. The least extensive surgical operation that will secure adequate compression is the operation of election. In many cases a sequence of procedures is neither indicated nor advisable. The character, location and extent of the lesion determines an operation of necessity. The general condition of the patient may and often does demand that it be performed in multiple stages. Better regret doing too little than mourn the death of a patient.

#### PROCEDURES

The procedures for collapse therapy are (1) artificial pneumothorax—unilateral, alternating or simultaneous bilateral, (2) intrapleural pneumolysis, (3) interruption of phrenic nerve conduction, temporary or permanent, (4) scalenectomy, (5) extrapleural pneumolysis with or without filling of the extrapleural space, and (6) thoracoplasty, partial upper or partial lower, as single stages or in sequence, with or without extrafascial mobilization of the lung, or complete, in multiple stages. The first four procedures leave the thoracic wall intact and with one exception (permanent phrenic nerve interruption) are revocable; the last two are compressing operations which alter the osseous structures of the thorax and are irrevocable.

*Artificial pneumothorax.*—The introduction of artificial pneumothorax marked a transition from the time-honoured passive and expectant treatment to the modern active or aggressive therapy of pulmonary tuberculosis.

Wherever the efficacy of timely pneumothorax is fully appreciated it is recognized as the most valuable adjunct to phthisiotherapy. It has become a standard form of treatment in modern sanatoriums everywhere, curing or arresting the progress of the disease not possible by expectant treatment alone.

Induced pneumothorax is the spearhead of a line of surgical attack to secure added local rest to the diseased area of the lung by procedures graded from early relaxation and temporary collapse to firm irrevocable compression.

It is unfortunate that these gradations are not generally recognized and understood. An appreciation of the gradation principle of collapse therapy is of utmost importance in the modern treatment of pulmonary tuberculosis. The advantages of timely graded collapse therapy are proved by the splendid results obtained in the treatment of resistant progressive and otherwise hopeless cases.

Artificial pneumothorax decreases the volume of the lung by the injection of controlled amounts of air through a needle introduced into a free pleural space. It may be relaxing, collapsing or mildly compressive. The more uniform and continuous, the more effective it will be. Refills are necessary at more or less regular intervals over a long period, demanding prolonged co-operation of the patient, which, for economic, business, social, temperamental or other reasons, is too often interrupted or altogether neglected. This leads to intermittence, early loss or complications. To obviate these the injection of oils was introduced. The safe use of oleothorax demands a greater degree of experience and judgment than does the use of simple pneumothorax.

An early, continuous, uniform and moderately relaxing pneumothorax is a prophylactic pneumothorax. It separates the visceral from the parietal pleura, prevents the formation of adhesions, relaxes and rests the lung, is conducive to contraction of early, soft, thin-walled cavities and healing of soft exudative or mixed productive pericavitary zones. Massive repeated hæmoptysis may be stopped. In bilateral lesions of a similar type, though of different intensity, it may be

induced on the two sides simultaneously or alternately. An early pneumothorax is not more dangerous to induce or difficult to control than is a later pneumothorax. It may obviate further measures for collapse.

The practice of inducing high degrees of plus pressure in order to secure attenuation of restraining adhesions, desirable as this may seem, is neither wise nor safe and frequently causes complications. Obliteration of the pleural space precludes pneumothorax. Adhesions may prevent the induction and maintenance of a satisfactory pneumothorax.

An incomplete pneumothorax, while it may not collapse cavities, does exercise a salubrious effect on the pericavitary lesions. It renders the pleura less sensitive, and the mediastinum more rigid and gives the heart and contralateral lung time to become adjusted to the altered intrathoracic pressure. The patient is thereby fortified and will better tolerate the necessary more formidable procedures for collapse. These should not be delayed. Prolonged pneumothorax treatment without diminution in the size of the cavities or continuing improvement of the lesions in the lung is not good therapy. It wastes valuable time, courts complications, imperils the final results and withholds from the patient other measures when these give assurance of success.

*Intrapleural pneumolysis.*—Closed intrapleural pneumolysis is the severance of restraining and tethering pleuritic adhesions through a thoracoscope by means of the electrocautery or coagulation.

Pleuritic adhesions are the greatest impediment to successful artificial pneumothorax; once formed they are usually progressive. If restraining adhesions are narrow, like cords or bands, or fan shaped and are long enough to permit the manipulation of the necessary instruments, they may be severed by intrapleural pneumolysis. Thus may an inefficient or partial pneumothorax be made efficient or complete.

A knowledge of the character and content of the adhesions and of their relation to the lung, pericardium and great vessels, especially at the apex, and to the thoracic wall is important, not only because of the effect they may exercise in keeping the cavity open and the lung expanded but also because of the possible danger of puncturing large vessels and the pericardium, and of tearing or eroding the cavity wall or the diseased lung during or subsequent to coagulation.

The number and disposition of adhesions cannot be adequately determined by x-ray study. The thoracoscope is of positive value in the study of intrapleural adhesions. The restraining effect of adhesions must be established before intrapleural severance is attempted.

At the apex of the thorax, the commonest site of resistant adherent cavities, where intrapleural pneumolysis would be most helpful, it is frequently impossible.

Open intrapleural pneumolysis does not require that the operator have training to acquire proficiency in interpretation of adhesions and dexterity in the use of specialized instruments. Open intrapleural pneumolysis is a more difficult and extensive operation. It has a very limited field for broad, short, isolated, tethering adhesions. A satisfactory closure of the pleura is not easy to accomplish.

*Interruption of phrenic nerve conduction.*—This paralyzes the diaphragm. It may be made temporary by crushing the main and accessory nerves, which may be repeated to prolong its effect when, after two or three months, the diaphragmatic function returns. Should a permanent paralysis be desired the main and accessory nerves may be cut or 4 or 5 inches of the stem evulsed. Permanent paralysis is occasionally indicated, especially when the lesion has so seriously compromised the lung that a restoration to function is nil. Alexander has proved that repeated temporary interruption is preferable and usually should precede a permanent phrenic interruption. Paralysis of one-half the diaphragm, even if there is no appreciable elevation, secures a continuous uniform relaxation of the lung. It is more resting than a pneumothorax. The inconvenience of refills, the variable tension and the waning of a pneumothorax are eliminated. Phrenic



nerve operations, while simple, have attending dangers, especially evulsion.

The indications are practically those for pneumothorax. Some authorities give interruption of the phrenic nerve preference, especially when continuing co-operation of the patient is doubtful.

Early temporary paralysis of the phrenic nerve will hasten and assure the benefits of general rest in recent thin-walled cavities with a pericavitary zone of the exudative or mixed type. It is positively indicated when a satisfactory pneumothorax cannot be induced, controlled or continued. It may supplement or intensify a unilateral pneumothorax without increasing the pressure. In the case of bilateral lesions it may be performed concomitantly on the worst side. The greatest benefits are in basal lesions. Midfield and infraclavicular lesions are almost equally controlled. A temporary interruption of the phrenic nerve is of advantage to retard reexpansion of the lung on abandonment of pneumothorax. It is effective in reducing the size of empyema cavities and in relaxing the lung, favouring closure of bronchial fistulas by contracting fibrosis. Massive repeated hæmoptysis is controlled by operation on the phrenic nerve. As a palliative procedure in terminal stages to assuage an exhausting cough it is superior to sedatives.

**Scalenectomy.**—In this operation the scalene muscles are resected close to their insertions in the first and second ribs. The unopposed action of these muscles elevating and horizontally rotating the upper ribs is very great. However, when the ribs and intercostal muscles below the third rib are intact, the effect of the scalene contraction disseminated over the entire thorax is greatly reduced.

Scalenectomy does reduce excursions of the upper ribs and rest the apex of the lung, but to a degree so small that its effect on the lesions in the apex is uncertain and often negligible. It is recommended to control the upper part of the thorax as a supplement or sequence to operations on the phrenic nerve. What a successful operation on the phrenic nerve cannot accomplish alone usually requires more than a supplementary scalenectomy.

**Extrapleural pneumolysis.**—This is the formation of an extrapleural or fascial space overcircumscribing the area of a cavity by finger or blunt dissection through an incision in the periosteal bed of a resected short segment of an overlying rib. The pocket thus formed is filled with some material to maintain firm selective compression of the cavity-bearing area. The compressing effect is immediate. If sputum is abundant overflow infection is a possibility. Firm fusion of the endothoracic fascia to the ribs, rupture of the cavity or hæmorrhage prevents completion of the operation. No satisfactory filling material has been discovered. Gauze has to be replaced, frequently causing considerable pain. Muscle, if sufficient is available, requires a large fenestra for introduction and fixation. It atrophies and contracts. Air necessitates refills. Bags inflated with water or compressed air leave a projecting tube which is conducive to infection. Paraffin is irritating and heavy and may cause pressure necrosis, erode and perforate the cavity wall or a free pleural space, shift or migrate out of position or be extruded through the incision. Theoretically ideal, practically it is uncertain. The presence of any foreign material in a wound is a menace. Its use is indicated for the very ill who cannot stand a limited or multiple stage thoracoplasty and have unilateral or bilateral disease with small to medium sized, chronic, thick-walled cavities in a dense fibrotic area with or without severe hæmoptysis.

Extrapleural pneumolysis with the use of gauze filling is most efficient in compressing dense residual fibrotic cavities that have failed to close by all other measures. Extrapleural pneumolysis occasionally is useful before a limited thoracoplasty. It is not easier to perform and is scarcely less shocking than a limited thoracoplasty. Though the compressive effect is selective and immediate, the delayed effect is uncertain.

**Thoracoplasty.**—The purpose of thoracoplasty is to secure collapse or active compression of a cavity-bearing area in the lung by means of the subperiosteal resection

of definite lengths of a variable number of ribs. It may be partial, limited to a few ribs, either the lower or the upper, or in stages including as many ribs as may be necessary to obtain adequate compression. The interval between stages is determined by the condition of the patient, time being allowed for the heart and lung to become adjusted to the altered intrathoracic condition and the diseased area in a measure to clear itself. The collapsing effect depends not so much on the length of the ribs resected as it does on the length of the stumps remaining, especially at the posterior aspect, where the resection must be made at the spine and may include the transverse processes. The number of ribs and the length of the segments to be resected are determined by the character, extent and localization of the disease in the lung, the stability of the mediastinum, the thickness of the pleura and the conformation and rigidity of the chest wall. In order to avoid secondary and difficult revision or corrective operations, total or subtotal resection of the first to the third or fourth rib should be performed in an upper stage, going well beyond the underlying diseased area of the lung. Whereas short segments and too few ribs may require additional stages, long segments of too many ribs may cause shock, too sudden and great a degree of compression, weakening of an extensive area of the thoracic wall, massive atelectasis seriously embarrassing respiratory and cardiac function, a dangerous degree of autotuberculinization and rapid local or wide dissemination of the disease.

Some excellent authorities, Casper, Semb and Overholt, at the time of thoracoplasty, especially in the upper stage, advocate and perform extensive mobilization of the lung. Casper leaves the wound partially open and firmly packs the area with gauze saturated with mild silver protein to secure firm compression. Redressing is required for a long time; convalescence is prolonged.

Carl Semb of Oslo, Norway, was the first to perform extrafascial apicolysis. He secures a concentric collapse and contraction of the entire cavity-bearing area of the upper part of the lung almost to the level of the hilus. In this operation resection of the upper rib segments is not so extensive as in the total or subtotal type of thoracoplasty. The extrafascial ligamentous attachments and adhesions to the lower cervical nerve roots, to the large vessels and to the anterior and posterior mediastinum are carefully severed by sharp and gauze dissection. The entire dome of the pleura is freed and then depressed. The first three intercostal muscle bundles are double ligated and then severed.

Extrafascial pneumolysis may be performed at the first upper stage or be a step in a revision or corrective operation for collapse of resistant cavities. The latter is more difficult but a safer procedure. With the total or subtotal resection of the upper ribs the collapse of apical and subapical cavities is more efficient and residual cavities are less frequent than in the resection of the limited segments of the former thoracoplasties.

Extrafascial pneumolysis is indicated in the case of apical and subapical cavities with dense fibrotic pericavitary zones without exudative foci.

The manipulation incident to mobilization of the lung and the too sudden and massive compression of an actively-diseased lung area are fraught with the danger of a local or widespread dissemination of the tuberculous process. The unsupported mobilized area of the lung beneath the limited deribbed upper portion of the thorax cannot be adequately supported. Paradoxical expansion, on coughing, of this unsupported lung is inimical to the clearing of the secretion from the diseased area. If the region should contain active foci or exudative areas, manipulation, displacement and active too sudden massive compression are prone to cause complications. The compressing effect is ideal, the greatest attainable. It is safer to do active forceful compression on a residual cavity in a densely fibrotic area with only low grade, if any, tuberculous infection by extrapleural gauze tamponade.

The indications for thoracoplasty are those for collapse therapy in general, when lesser measures have failed or the temporary collapsed cavities reopen and quiescent areas become reactivated. The degree of

fibrosis and contraction deformity is an index of the rigidity of the mediastinum and the local resistance of the lung tissue. A rigid mediastinum gives assurance of cavity compression and security against mediastinal flutter and displacement.

Contra-indications to collapse are fresh, recent exudative lesions in the opposite lung, especially near the base; severe asthma, emphysema, active or decompensated heart disease, uncontrolled diabetes and

tuberculosis in other organs are, in proportion to their activity, unfavourable complications. Severe anaemia, rapid pulse and low blood pressure are warnings of danger; they prejudice but do not preclude surgical collapse.

Delay in diagnosis has been and is the chief obstacle in the control of pulmonary tuberculosis.

Delay in instituting the proper procedure for collapse compromises and may defeat all efforts to cure.

## Reviews

**NEUROLOGY.**—By S. A. Kinnier Wilson, M.A., M.D., D.Sc. (Edin.), F.R.C.P. Edited by A. Ninian Bruce, F.R.C.P. (Edin.), D.Sc. (Edin.), M.D., F.R.S., Lieut.-Colonel, R.A.M.C. Volumes I and II. 1940. Edward Arnold and Company, London. Pp. xxxvi plus 752 in volume I and Pp. xxvii plus from 753 to 1838. Illustrated. Price, £4-4-0 for two volumes

THESE two volumes are the outcome of a life's work on neurology. Dr. Wilson died before his task was finished and Dr. A. Ninian Bruce has completed it for him.

As regards the general arrangement a complete table of contents is provided in volume one along with a list of abbreviations for nearly three hundred periodicals from which references are made. Volume two which is considerably larger is provided with a table of contents referring to it alone. The same list of abbreviations is provided, but in addition at the end of this volume there is an index of authors containing about five thousand names, and an extremely useful subject index of seventeen pages.

The volumes are divided into ten parts. The first deals with toxic-infective diseases of the nervous system, and includes meningitis, fevers, disseminated sclerosis, and neuritis in its many forms. In the treatment advocated for epidemic cerebro-spinal meningitis, serum by the intrathecal route supplemented by vaccines is recommended, but there is no mention of treatment by sulphonamides. This is rather surprising in view of the increasing number of successes reported by the use of chemotherapy alone.

Part two deals largely with neuro-syphilis, but there are also chapters on chorea, tetanus, and diphtheria. Subjects of more tropical interest such as leprosy, rabies, and malaria, are also included. Boerhaave's account of 'dog madness' or hydrophobia written two hundred years ago is reproduced in the chapter on rabies and is remarkable for its accuracy of observation.

Part three concludes volume one with chapters on poisoning by morphia, cocaine, alcohol, and lead. The final chapter on heat stroke is very brief.

Parts four, five and six deal with degeneration or toxic-degenerative disorders, diseases of vascular origin, and tumours of the nervous system respectively, and are masterpieces of completeness and lucidity.

*Metabolic and deficiency disease states* is the title of part seven. It includes subacute combined degeneration of the spinal cord, pellagra, and beri-beri. The chapter on pellagra is not up to date. There is no mention of nicotinic acid treatment or of any of the recent work in the United States from 1937 onwards, and no reference of later date than 1935.

The last three parts are devoted to congenital anomalies, diseases of uncertain nature, and the neuroses, all of which are excellent.

One cannot help admiring the labour, patience, and skill which were necessary for the preparation of the material for these two volumes, and Dr. Wilson must have possessed, as stated in the foreword, 'an encyclopaedic mind'. They contain a wealth of detail which can be found nowhere else. Unlike many reference books the subject is presented in an interesting way

with numerous quotations from personal experience. In the next edition more reference should be made to recent work. The many excellent photographs add greatly to the value of the work which will be welcomed not only by neurologists but by those in general practice as well.

J. G.

**LEPROSY.**—By Sir Leonard Rogers, K.C.S.I., C.I.E., M.D., F.R.C.P., F.R.C.S., F.R.S., I.M.S. (Retd.), and E. Muir, C.I.E., M.D., F.R.C.S. (Edin.). Second Edition. 1940. John Wright and Sons, Limited, Bristol. Pp. xii plus 260. Illustrated. Price, 15s.

THE first edition of this book appeared in 1925. At that time there was no good up-to-date book on leprosy in English or in any other language, and this book went a considerable way towards filling the need. It summarized knowledge of the subject up to that time, and it helped to stimulate interest in leprosy all over the world. It had certain shortcomings, the chief of which was the absence of any list of references or bibliography.

The last fifteen years have seen a great increase in knowledge of all aspects of leprosy, and to this the two authors have made considerable contributions. During this time no other book covering the same ground has appeared in English, and it is therefore natural that a new and revised edition should be called for.

The new edition contains forty pages less than the old one, and like the old one it is divided into six sections, headed 'history and distribution', 'epidemiology and communicability', 'prophylaxis', 'aetiology', 'clinical' and 'treatment'.

To the first three sections only minor alterations have been made and some data have been added, particularly concerning the distribution of leprosy in the world. The main arguments and conclusions remain the same. Some people may consider that the comments made on the policy of anti-leprosy work adopted in the past in some countries are unnecessarily critical. The author of these sections, however, often expresses satisfaction with recent modifications of such policy. He stresses the importance of isolation of infectious cases, of limiting the use of compulsion as far as possible, and of treatment of isolated and other patients, in order to make measures of prophylaxis more popular and effective.

On reading a book like this, one naturally reads with special care statements about the country in which one's work lies. We would agree with most of the statements made about leprosy in India but there are certain statements which appear to us to be misleading. The estimated number of lepers in India is given as 500,000. Most recent estimates based on actual surveys are much higher than this. The map on pages 24 and 25 does not make clear the distribution of leprosy in India, nor does the discussion on leprosy in India which follows. The statements quoted from Santra regarding fish eating in Bankura (Bengal, not Bihar as stated) and parts of Burma where leprosy is very common appear to us to be misleading for we have found that fish eating is equally common in other



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adjacent areas where leprosy is much less common. Santra's report, that leprosy is less common in single-caste villages, is interpreted as indicating the influence of promiscuity in spreading leprosy in villages with several castes; but it appears to us that in single-caste villages, the people will mix more freely, because of the absence of caste restrictions.

In the section on prophylaxis on page 122 the following statement is made; 'The only way to reduce the incidence of leprosy rapidly is to trace and examine every few months over a period of at least five years, any person who has been in close contact with any known infective leper. A large proportion of the infections from each case so discovered in the earliest stage can be cleared up and prevented from going on to an infective stage.' This statement is made as though it were a generally accepted opinion, and neither in this section nor elsewhere is any mention made of the opinion of some experienced workers in certain countries (e.g., Rodriguez) that treatment will not prevent non-infectious cases from becoming infectious.

The other three sections, 'aetiology', 'clinical' and 'treatment', have been much more thoroughly revised along the lines of Muir's other publications, since the last edition. The system of classification and the terminology of the International Leprosy Congress, Cairo 1938, have been adopted throughout.

These three sections, which in the old edition occupied 147 pages, now occupy only 106. This condensation does not prevent them from being really useful surveys of these subjects. We think, however, that the descriptions of the clinical appearances and distribution of the different types of lesions, and of histopathology might have been better arranged, and the importance of the patient's age in prognosis might have been more fully discussed and emphasized.

Certain criticisms might be made regarding the description of the bacillus of leprosy. For example, it is stated that apart from its appearance in acute exacerbations of the disease the bacillus is a uniformly stained rod. Our experience is that diphtheroid forms, 'sporelike' forms, etc., are seen in all phases of the disease, although perhaps in somewhat varying proportions.

On page 167 the census figures of India are quoted as indicating that 0.4 per cent of cases of leprosy are under the age of three, and while some doubt is expressed on this point, an argument is based on the possible truth of this finding. In our experience leprosy is rare in such young children.

Seventy excellently reproduced photographs are printed in 34 plates at the end of the book, an arrangement which facilitates the binder's but not reader's task. We know, however, the difficulty of printing art plates opposite to, or near, the page of the book which they illustrate, and there is much to be said for the arrangement adopted here. The book contains a good index.

Although numerous authors are quoted by name, sometimes with the date, there are very few complete references given. In a book of this kind a complete list of references would be very long, but we think that its value as a work of reference would have been considerably enhanced by the insertion at the end of each chapter of a select bibliography indicating the most important publications on the subject of the chapter.

The book is a very useful general survey of leprosy, the only one in the English language which attempts to cover the whole field of leprosy. It is excellently printed and bound.

**A TEXTBOOK OF OCCUPATIONAL DISEASES OF THE SKIN.**—By Louis Schwartz, M.D., and Louis Tullipan, M.D. 1939. Henry Kimpton, London. Pp. 799. Illustrated with 116 photographs. Price, 45s.

ALTHOUGH references to industrial skin diseases can be traced back to Paracelsus, according to the opening paragraph in chapter 1 of this book, it is only in

relatively recent times that the endless possibilities in this respect have been fully recognized. The importance of skin eruptions from contact with chemicals and other substances used in industry is steadily expanding, as new discoveries in processes of manufacture lead to the establishment of new industries.

This publication is an extremely valuable one as a book of reference for dermatologists, medical officers of health, and doctors engaged in the care of employees of large industrial concerns, because in it they are almost certain to find a reference to any problem of industrial dermatosis they are likely to encounter. Simply reading the contents list of the 45 chapters is an education in itself in revealing the innumerable possibilities in this special aspect of dermatology.

P. A. M.

**SURGERY OF THE EYE.**—By M. Wiener, M.D., and B. V. Alvis, M.D. 1939. W. B. Saunders Company, Philadelphia and London. Pp. 445, with 396 illustrations. Price, 37s. 6d.

THE book is written primarily to supply a handy atlas for the student of ophthalmology and the practising ophthalmologist to which to refer for information on the surgical treatment of ocular defects and disease. As most surgical books on the eye are insufficiently illustrated the authors have endeavoured to bear this in mind and all the operations selected have therefore been clearly and profusely illustrated by serial drawings and diagrams.

The book consists of 419 pages with as many as 396 illustrations. It is divided into 18 chapters in which the authors discuss general considerations, the preparation of the patient, anaesthesia, pre-operative preparation, post-operative care, paracentesis, cataract, glaucoma, operations on the retina and sclera, intra-ocular foreign bodies, operations on the cornea, removal of eye, operations on the conjunctiva, operations on the lids and socket, ptosis, operations on muscles of eye, and finally operations on the tear sac.

The chapters on cataract and glaucoma are excellent and will be of great interest to ophthalmic surgeons working in India. The book is excellently produced and the subject-matter is written in a simple, clear style and is easy to follow.

There is little to find fault with and the authors are to be congratulated on their production and we hope it will be extensively read. We strongly recommend the book, and as a help and guide to the ordinary eye operations we have yet to find its equal.

E. O'G. K.

**THE SEXUAL PERVERSIONS AND ABNORMALITIES.**—By Clifford Allen, M.D., M.R.C.P., D.P.M. 1940. Oxford University Press, London, Humphrey Milford. Pp. xli plus 193. Price, 7s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

THE trouble with sexologists, including the author of this book, is that they invariably omit to define or even consider what they mean by the terms 'normal' and 'abnormal' in relation to the sexual impulse. By informing his readers that he himself is 'fortunate to be normal', we see him disappear into the abyss into which so many other sexologists have fallen, including Freud himself. No one can deny that psychoanalysis has correctly understood the urgency of sexual needs and has perceived the possibility of cure through the reasonable satisfaction of these needs, but it has failed to realize the necessity for a revision of the ridiculous way in which our present conventions look upon the manifestations of sex. To attain a more scientific theory of sex, psychoanalysts have got to realize that the sexual mechanism is more important than the sexual object. A normal instinct is supposed to be one which leads the individual to a person of the opposite sex. But we know that this so-called normal object-choice is only necessary for the function of reproduction, and has nothing to do with the instinct of sexual pleasure which demands nothing more than its mechanical satisfaction. The nature of normal

sexual satisfaction is no easier to understand. The function of reproduction can scarcely be carried out except by coitus; but pleasure may be completely attained by any other method, sometimes even more completely. Like Freud, Dr. Allen appears to imagine that the sexual instinct puts itself at the service of reproduction. We might just as well say that taste puts itself at the service of the stomach to aid the function of nutrition. Like the majority of sexologists, Dr. Allen appears to be unaware of what any intelligent man-in-the-street knows, namely, that nine times out of ten, sexual pleasure pursues its own end and is not at all concerned with reproduction, is indifferent to it, and, in many individuals, is even compatible with a strong conscious desire to avoid reproduction. In the light of these considerations we are confronted with the solution of the problem as to what constitutes disease; what is 'normal' and what is 'abnormal'. As the author of that penetrating study of sex entitled, *Sex Life and Sex Ethics*, has pointed out, a mind that was not dominated by thousands of years of anti-sexual taboo would have no difficulty in answering this question, and in making the necessary distinctions without resort to any superfluous psychological complications. Such a mind, says the author of *Sex Life and Sex Ethics*, would very likely make the three following formulations: (a) That the exercise of the sexual organs for the avowed purpose of procuring sexual pleasure, and ultimately also for the purpose of reproduction, is natural, normal, proper, legitimate, and indeed necessitated by the demands of our constitution: (b) That failure to exercise these organs, as a consequence either of voluntary abstinence or of external circumstance (chastity, legal prohibition, etc.), is, on the contrary, an artificial, abnormal, unhealthy and unpleasant state: (c) That sexual pleasure, the immediate aim of sexual activity, is obtained through an appropriate mechanism. This mechanism presents certain variations; but, so far as the general principle is concerned, and except for possible differences in the degree of pleasure obtained, it is independent of the quality (and, above all, of the moral value) of the methods or the partners employed for setting it in action; it can function just as well without a partner (as in onanism), or with any kind of partner (as in homosexuality).

O. B-H.

**CANCER OF THE LARYNX.**—By Chevalier Jackson, M.D., Sc.D., LL.D., F.A.C.S., and C. L. Jackson, A.B., M.D., M.Sc. (Med.), F.A.C.S. 1939. W. B. Saunders Co., Philadelphia and London. Pp. x plus 309, 189 illustrations with 5 plates in colour. Price, 40s.

THE name of Chevalier Jackson is an honoured one in the annals of laryngology. No one is probably better fitted than he to write an authoritative treatise on carcinoma of the larynx. It is particularly gratifying that in this work he is assisted by his worthy son.

This book of 318 pages is very well planned and consists of three parts. Part I, comprising 12 chapters, deals with procedures. Great emphasis is laid on early diagnosis and all the diagnostic steps are clearly described. The difficult subject of treatment is presented in a masterly fashion. The choice of treatment for the particular case is clearly indicated but here, as in diagnosis, experience is likely to be the main deciding factor. Part II, dealing with general considerations, is replete with clinical facts, data and statistics which are not available elsewhere. The chapters on aetiology and its corollary prophylaxis are of particular interest. Part III deals with the history of cancer of the larynx, affording, in the authors' words, 'lighter reading for the reader', but in reality there is much food for serious thought in this section. The historic case of the then Crown Prince of Germany is discussed in some detail. The controversy regarding Sir Morell Mackenzie's responsibility in an unfortunate surgical episode is now discussed from the medical point of view.

This is an excellent book not merely for the specialist but also for the general practitioner. The printing, get-up and illustrations are all first rate. There is a complete bibliography in addition to a useful index.

P. N. R.

**POISONS: THEIR ISOLATION AND IDENTIFICATION.**—By Frank Bamford, B.Sc. 1940. J. and A. Churchill, Limited, London. Pp. viii plus 344, with 21 illustrations. Price, 18s.

THIS volume has been designed as a practical handbook for chemists dealing with the detection and identification of poisons in the laboratory. It is therefore full of practical details required in this connection, whilst theoretical considerations are included only where they are absolutely necessary. In the foreword written by such an eminent authority in forensic medicine as Professor Sydney Smith, Regius Professor in Edinburgh University, the volume has been described 'to be the product of a practical, highly skilled specialist in toxicological analysis, which can be recommended with complete confidence to analysts'. With this view we agree. The subject-matter is well arranged so as to be easily available for purposes of reference and the book is written in a lucid style. The different groups of poisons have been dealt with in detail and a section has been added on drugs of addiction. We can recommend this volume to those dealing with medico-legal problems in this country.

R. N. C.

**DISEASES OF THE DIGESTIVE SYSTEM: A TEXT-BOOK FOR STUDENTS AND PRACTITIONERS.**—By Eugene Rosenthal, M.D. 1940. Henry Kimpton, London. Pp. xii plus 394, with 234 illustrations including 104 in colour, and 16 plates. Price, 42s.

IN this volume a teacher of distinction in the University of Budapest presents a technique of teaching which is both novel and effective. The training of the medical student nowadays entails a great deal of strain, even for the most talented. In an appreciative preface, Dr. Pulvertaft, reader of Pathology in the University of London, speaks very highly of the author's method of instruction, with diagrams and geometrical forms of illustrations.

This book consists of five chapters the first of which deals with diseases of the oesophagus. Chapter 2, consisting of nearly 200 pages, is devoted to diseases of the stomach and intestinal tract. In chapter 3 the diseases of the liver and biliary tract are discussed in some detail. The treatment in each condition is very clearly indicated. In the two concluding chapters diseases of the pancreas and peritoneum are dealt with.

This is a most instructive book and it is written in simple English. The illustrations are excellent, numerous and original. The printing and get-up are very good indeed. This is a book which we can strongly recommend to the general medical practitioner. A useful index is appended.

P. N. R.

**MIDWIFERY: PRINCIPLES AND PRACTICE FOR PUPIL MIDWIVES, TEACHER MIDWIVES, AND OBSTETRIC DRESSERS.**—By R. Christie Brown, M.B., M.S., F.R.C.S., F.R.C.O.G., and Barton Gilbert, B.Sc., M.D., F.R.C.S., M.R.C.O.G. With the Infants' Section by Richard H. Dobbs, M.B., B.Ch., F.R.C.P. 1940. Edward Arnold and Company, London. Pp. viii plus 796. Illustrated. Price, 15s.

DESIGNED for midwives and the teachers of midwives this book adequately fulfils its purpose.

It is written in easily understandable syntax, and stresses the basic principles of biology as its most important factor.

A certain amount of elementary embryology, chemistry and physics is gone through and explained. This is a somewhat unusual departure, but it is



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In the section on eclampsia a dogmatic statement is made that the disease usually develops in women who eat excessively of meat. This statement, however, cannot be acquitted of error when it is a well-known fact that eclampsia is very common in India and China where the women are for the most part, entirely non-meat eaters. There are many diagrams in the book which, although of a simple nature, are well drawn and illustrate with clarity the conditions described.

An admirable book is the verdict on this volume.

**AN INTRODUCTION TO MEDICAL GENETICS.**—By J. A. Fraser Roberts, M.A., M.B., D.Sc., F.R.S.E. 1940. Oxford University Press, London, Humphrey Milford. Pp. xxiii plus 266. Illustrated. Price, 15s. Obtainable from Oxford University Press, Bombay and Calcutta.

This excellent book is a happy departure. Genetic inheritance is explained directly by showing the movements of the genes. The traditional cryptic symbolism has been kept out nearly throughout. It appears in an insignificant rôle towards the end where short is represented by *tt* as would have been better. The over-worked American fruit-fly and cruditè formulæ have also been kept out. Yet medical men interested in genetics have been presented with all they need.

The price perhaps could be lower. The granulated cloth of the binding to which insects are very partial is a disadvantage in the tropics.

S D S G

**AIDS TO PSYCHOLOGY.**—By John H. Ewen, M.R.C.P. (Edin.), D.P.M. Second Edition. 1940. Baillière, Tindall and Cox, London. Pp. vii plus 176. Price, 3s. 6d.

**AIDS TO PSYCHIATRY.**—By W. S. Dawson, M.A., M.D. (Oxon.), F.R.C.P. (Lond.), F.R.A.C.P., D.P.M. Fourth Edition. 1940. Baillière, Tindall and Cox, London. Pp. vii plus 320. Price, 4s. 6d.

BOTH these little books are written by doctors for medical students—undergraduate or post-graduate. That medical training has reached a point whereat psychology is admitted to the rank of a 'subject', shows that the teaching of psychopathology and psychiatry is becoming a serious affair. Without undue optimism one is at liberty therefore to presume that in a generation or two the famous dictum of Trousseau, 'there are no diseases but only diseased persons', has a hope of attaining recognition. In the list of works to which the author of *Aids to Psychology* states in his preface he is under an obligation, it is remarkable to observe that he makes no mention of the work of Professor C. Spearman 'Psychology down the Ages', a book which is certainly the most eminent textbook of psychology in English and possibly in any other language. Dr Ewen is evidently a loyal disciple of the late Professor McDougall with the result his psychology is all-too-human. On page 55 we are told that one of the differences between Natural Man (whatever the term 'natural' may connote) and other Mammals is that man has 'foresight of the future in accordance with the past'. The present situation in Europe would hardly support this statement. To the researches of animal psychology no reference is made. 'Gestalt' psychology is considered and dismissed in two paragraphs on the last page in the book, but in such a fashion as to leave the reader with a vague notion that 'there is something in it'. In case Dr Ewen has overlooked Professor McDougall's opinion on Gestalt psychology, it is as follows—'I would submit that no one of the principles of Gestalt psychology is new, except one (isomorphism), which is, I think, demonstrably false'. In other words, the medical student who reads this book is not getting a fair deal. Of course, it is possibly beyond human achievement to give any one a fair deal in psychology in what is no more than a cram-book. This remark applies more or less to the book of Dr Dawson which in spite of the

fact it is in its fourth edition, is lamentably behind the times. It is even more of a cram-book than the book of Dr Ewen, and as such its sale should be prodigious. That the book is particularly devised to help students to pass the examination for the Diploma of Psychological Medicine and is now in its fourth edition, seems rather to reflect on the scope of the D.P.M. Dr Dawson appears to regard Kraepelin's work on dementia praecox to be still of practical value, although Kraepelin's original conception is now held to be more or less bankrupt. Dr Dawson makes no mention of 'psychobiology' nor of the concept of the somatopsychoses. In the matter of therapy, occupational therapy is hardly touched on while in regard to mental hygiene the name of Clifford W. Beers is not even mentioned. If Dr Dawson is representative of psychiatry in Australia, Australian psychiatry has a good deal of lee-way to make up.

**THE PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE: A UNIVERSITY OF TORONTO TEXT IN APPLIED PHYSIOLOGY.**—By Charles Herbert Best, M.A., M.D., D.Sc. (Lond.), F.R.S., F.R.C.P. (Canada), and N. B. Taylor, M.D., F.R.S. (Canada), F.R.C.S. (Edin.), F.R.C.P. (Canada), M.R.C.S. (Eng.), L.R.C.P. (Lond.). Second Edition. 1939. Baillière, Tindall and Cox, London. Pp. xvi plus 1872. Illustrated. Price, 55s.

THE fact that this book, which was first published in 1937, was reprinted four times is in itself a sufficient proof of its popularity and utility. The second edition appeared in September 1939 and has been thoroughly revised and enlarged. A new section has been added on the physiology of the special senses and the whole of the subject matter has been brought up to date. This is a most excellent book which puts in very simple and easily comprehensible language the applicability of modern concepts of physiology in the treatment of disease. We strongly recommend it both to students and practitioners in this country as a perusal of it will enable them to understand the physiological basis of scientific medical practice which is the only way they can equip themselves for successful careers.

R N C

**AIDS TO MATERIA MEDICA.**—By G. H. Newns, M.D. (Lond.), M.R.C.P. (Lond.). Second Edition. 1939. Baillière, Tindall and Cox, London. Pp. vii plus 171. Price, 3s. 6d.

THE students aid series is designed with the object of assisting medical students reading for examination. The second edition of *Aids to Materia Medica* has been thoroughly revised and includes the new drugs contained in the British Pharmacopœia Addendum 1936. The preparations of the drugs are clearly given and their pharmacological actions are concisely stated. The book is reasonably priced and will be useful to Indian students.

R N C

**AIDS TO PRACTICAL NURSING.**—By M. Houghton, S.R.N., S.C.M., D.N. (Lond.). Second Edition. 1940. Baillière, Tindall and Cox, London. Pp. xii plus 308, with 36 figures. Price, 3s. 6d.

THIS book is essentially practical and is of everyday use to nurses in training. If the other parts of this 'Aids' series is of equally high standard, I shall have no hesitation in recommending my pupils to collect this inexpensive series for their progressive studies.

R C

**A POCKET MEDICAL DICTIONARY.**—Compiled by Lois Oakes, S.R.N., D.N. (Lond. and Leeds). Assisted by Thos. B. Davie, B.A., M.D. (Liverpool), M.R.C.P. (Lond.). Fourth Edition. 1940. E. and S. Livingstone, Edinburgh. Pp. xx plus 409. Illustrated. Price, 3s. 6d. Postage, 2d.

THIS dictionary should be in the possession of every training and post-graduate nurse. Its definitions are simple and comprehensive, and the book is completely up to date with the revised medical terminology.

R C

**LIPPINCOTT'S QUICK REFERENCE BOOK FOR NURSES.**—Compiled and arranged from Various Sources. By Helen Young, R.N. With the Assistance of G. A. Morrison, R.N., and M. Elliot, R.N. Fourth Edition. 1939. J. B. Lippincott Company, Philadelphia and London. Pp. 557. Price, 9s.

THE book comprises a very well-thought-out scheme for grouping nursing procedures, thus providing a time-saving guide for the busy nurse.

R. C.

**HORMONES IN INVERTEBRATES.**—By Bertil Hanstrom. 1939. Oxford University Press, London. Pp. ix plus 198, with 13 plates. Price, 12s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

THIS is the first volume to appear in the new series of monographs on animal biology which are being published by the Oxford University Press under the general editorship of Dr. G. R. De Beer. The importance of hormones in man and higher animals has received particular attention during recent years, and the part which they play in the proper functioning of the organism by chemical correlation has been fully appreciated. Lately, attention has also been paid to the part the hormones play in the economy of the invertebrates, and biologists will be grateful to Professor Bertil Hanstrom, whose work in connection with invertebrates is well known, for presenting a summary of the present knowledge on the subject. The difficult task before him has been accomplished with great skill and he has given in very lucid and easily comprehensible language the various functions which these hormones perform. An account of the anatomy and physiology of the excretory organs in different invertebrates is given and their connection with different hormones is indicated. There are interesting sections on the influence of vertebrate hormones on invertebrates and invertebrate hormones on vertebrates. Other sections which will be of interest to the biologist are hormonal regulation of colour changes, retinal pigment migration and neuro-secretory organs. A comprehensive list of references is given at the end. The book is priced low and will greatly interest biologists.

R. N. C.

**COMMON MISTAKES OF SURGERY IN INDIA AND HOW TO AVOID THEM.**—By Lieut.-Colonel A. N. Palit, O.B.E., F.R.C.S. (Edn.), M.R.C.O.G., I.M.S. (Retd.). 1940. Book Company, Calcutta. Pp. xx plus 382. Illustrated. Price, Rs. 5

THIS book is intended to be a practical handbook for the young surgeon, the general practitioner, the hospital medical officer and the surgically-minded student. The author has written the book with a laudable object and we hope that his desire may be fulfilled. It contains an appreciative foreword by Major-General Mills, the present Surgeon-General with the Government of Bengal.

P. N. R.

#### OTHER BOOK RECEIVED

**An Introduction to the Principles and Practice of Homœopathy.** By Charles E. Wheeler, M.D., B.S., B.Sc. (Lond.). Second Edition. William Heinemann (Medical Books), Limited, London (99, Great Russell Street, W.C.1). Pp. viii plus 344. Price, 15s.

## Abstracts from Reports

### ANNUAL REPORT OF THE KASHMIR MEDICAL MISSION OF THE CHURCH MISSIONARY SOCIETY FOR THE YEAR 1939

THE beginning of medical missionary work in Kashmir was made by Mrs. Robert Clark, wife of Rev. Robert

Clark, just seventy-five years ago in the summer of 1864. The urgent need for medical relief may be judged by the fact that Mrs. Clark, though not a doctor, often treated as many as a hundred patients in a day in Srinagar. The following year, Dr. Elmslie our first mission doctor was appointed, and since then there has been a continuous succession of doctors to carry on the work.

The past year has been a difficult one for our hospital, but the work has been well maintained in all departments: medical, surgical, pharmaceutical and evangelistic. That the hospital has kept up its popularity is shown by our statistics, showing the numbers of in-patients admitted to this hospital for the last 58 years.

As usual we had to treat a great variety of medical and surgical cases, many of them suffering from grave and serious disease. Of various medical diseases, heart disease is one of the most prevalent with which we have to deal, and a large proportion of those who seek our aid for this trouble come in an advanced stage of the disease and, to do any real good, admission to the wards is essential.

Of surgical troubles, bone disease is one of the commonest with which we have to deal. It is due largely to deficiency in diet. These patients occupy our beds for longer periods than any other class of sufferers. Often after a successful major operation in which all diseased bone is removed, it may be six months or more before the patient is fit to return home. There can I think be no doubt that many of these patients receive not only physical healing but a real moral and spiritual uplift while in our wards. A number of these patients before admission to hospital have had their disability for many months or even years, and prolonged treatment by 'Hakims' has failed them, and they come to us sad and dispirited.

At least some Kashmiris are grateful for the work of this hospital. It was only about a year ago that a relative of one of Dr. Rawlence's patients gave us two hundred or more young trees which were planted in our hospital grounds. A number of Kashmiris have for some years been giving subscriptions and donations to the hospital, and at least one well-known Kashmiri business man has given a banker's order for a monthly donation to our funds. On this very day, a Kashmiri has asked the writer to accept Rs. 500 for this hospital but he has stipulated that the gift must be kept anonymous.

One way in which our hospital has increased its usefulness in the last four years has been the thorough training of dispensers, not only for our own hospital but also for others. During the last four years eight candidates have passed the first dispensers' examination and five have completed the course and passed the second and final examination. Four young men who qualified as dispensers have left and are now well able to do useful and very responsible work in various parts of India.

There has been considerable progress in recent years in the prevention of epidemics by the public health authorities, and the widespread epidemics of smallpox, cholera, dysentery and typhoid, which used to occur, now no longer devastate the country. But tuberculosis is a modern plague which needs to be tackled on a widespread scale, and with great vigour. The Kashmiri has a poor resistance to tuberculosis, and it causes a heavy mortality, both among the young and old.

The solution to the health problem of Kashmir, like any other country, depends largely on its diet and food supply, and clean and healthy habits of its people, and there is no reason why in Kashmir the people should not be one of the healthiest in the world. The land is so fertile that almost any crops and fruit will grow abundantly. The climate is exceptionally good, and the natural resources are almost unlimited.

In the fight against disease, success depends largely upon having a supply of good and efficient drugs ready at hand for immediate use. In this hospital we endeavour to keep abreast with modern medicine and treatment, and in the past we have had every reason to be proud of its record. Owing to the war, it is becoming

A specialist in Tropical Medicine, addressing a meeting of eminent malariologists, recently stated :

*"I am definitely of the opinion that prophylactic quinine does prevent actual attacks of malaria. Once or twice the experiment was tried of withholding prophylactic quinine for a week or two from large groups of men. This was followed by such increases in the sickness rate from malaria that a rapid return to the prophylactic dose was made."*

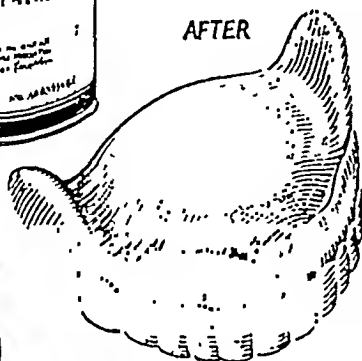
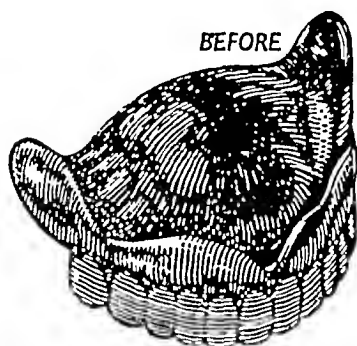
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increasingly difficult to obtain certain drugs, partly owing to difficulties in transport from England, and partly on account of the large increase in cost. We hope that those who have supported us in the past, will do so with renewed generosity in the future, and help the medical and surgical work of the Kashmir Mission Hospital to be carried on in these difficult days.

#### THE NINETEENTH ANNUAL REPORT OF THE RAMAKRISHNA MISSION SEVASHRAM (CHARITABLE HOSPITAL), RANGOON, FOR THE YEAR 1939

Born in the indoor and outdoor sections there has been a rise in the number of patients. The following figures for the last five years will give an idea of the extent the public has used the hospital and there is every reason to anticipate further increases in the coming years.

Year	Indoor	OUTDOOR		Total
		New	Repeated	
1935	3,746	79,448	116,303	199,497
1936	4,083	85,423	137,829	227,335
1937	4,375	88,418	150,951	243,744
1938	4,701	98,190	160,634	263,525
1939	5,263	104,591	199,100	308,954

The death rate was 5.25 per cent.

The patients requiring x-ray examination were sent to the Rangoon General Hospital and to the tuberculosis clinic of the Corporation of Rangoon.

Wassermann and other important tests were done by the Pasteur Institute of Burma and the management takes this opportunity of offering the institute and its Director, its heartiest thanks for their co-operation. Besides these, 8,260 tests were carried out by the laboratory of the hospital.

With the addition of 18 beds in the Nanigram maternity ward and 12 beds in the segregation ward the total number of beds available is 200 of which 56 are for the females.

In the year under review there were 15 nurses for the female wards and 21 male workers did nursing in the male wards besides the *Swamis* and *Brahmacharins* of the Ramakrishna Order who held charge of nearly all the responsible posts so far as the indoor general management was concerned. Sister Anderson of the St. John Ambulance Brigade, with her band of devoted workers, helped in the female wards and out-patient departments; but for their help, it would have been difficult to manage the ever-increasing demand made on these departments and the management takes this opportunity of conveying its heartiest thanks for their labour of love.

The managing committee met every month for transaction of business. The attendance was very satisfactory.

The opening of the maternity and segregation wards marked a great improvement in the hospital. The maternity block with its clinic has become very popular and is rendering valuable service to the poor public of this locality. It was opened on the 20th November, 1939, by His Excellency the Governor of Burma.

#### THE SECOND PROGRESS REPORT OF THE SAIDAPET HEALTH PROJECT

The Second Progress Report of the Saidapet Health Project, recently published, gives a survey of 1939, along with detailed reports of the various activities of the association.

The fact that this is only the second report may suggest to some, that this work has been going on for only two years. It was actually started as long ago as 1932, but the promoters have been content to concentrate on making sure foundations before issuing a public report.

The report begins with a review of the spade-work, when decisions had to be taken as to how best the objective of Saidapet—'the cleanest and healthiest town in South India by 1950'—could be reached; which of the prevalent diseases most urgently required investigation in the actual situations where they occur; how public apprehension, if it were to be leprosy, could be disarmed; what staff would be needed to visit the 3,000 homes and correlate the information gained, and lastly but most important, how the scheme was to be financed.

It was decided to concentrate upon the relief of leprosy—the Silver Jubilee Children's Clinic was opened in 1937—and to seek the interest and co-operation of the people through an efficient maternity and child-welfare centre, which was opened in 1934.

#### Maternity and child-welfare centre

During the year ending 30th April, 1939, 1,575 women attended the antenatal clinic, though less than one-sixth of that number were delivered by a member of the staff; the reason for this is that many pregnant women, assured at the clinic that their case is normal, are at the last moment persuaded to accept the care of the traditional midwife. Of the 208 cases attended during childbirth (146 in the centre and 62 at home) six babies were still born or died, while the maternity mortality rate was *nil*. In July a whole-time lady medical officer was appointed.

#### Leprosy

With regard to the leprosy investigation, three main objects can be defined:—

(1) Causes of the development of leprosy in children.

(2) The types of leprosy in children.

(3) The significance of the various types of child leprosy, and a study of the factors which influence the development of the more serious types.

The report shows that the clinic is becoming increasingly popular, for parents bring their children with even the slightest blemish, to ask whether it may be due to leprosy, and it reveals the following interesting findings. Half the children in the observation group are 5 to 9 years of age and a third are 10 to 14 years, whereas in the treatment group two-thirds of the children are aged 10 to 14 years. When an attempt was made to trace the source of infection, divisions were made into intra-familial (room and house) and extra-familial (street and school) contacts. Space forbids reproduction of all the figures concerned, but nearly half of the sources of infection of the 284 neural cases were definitely traced, and nearly two-thirds of the lepromatous ones. The report frequently emphasizes that the greatest danger is contact with open cases, and that where this contact is maximum there appears to be the greatest risk of acquiring serious-type leprosy.

At the assessment made in July 1939, out of a group of 145 children under observation only, 64 were found to be improved, 66 stationary and 15 worse. This group does not contain lepromatous cases which are classified in a separate treatment group; of their total of 43, 17 became negative, 11 improved (while remaining positive or open), 2 were stationary and 13 worse, while the corresponding figures for 49 'N1' cases under treatment were 35 improved, 4 stationary and 10 worse.

An experiment was carried out to observe the effect of the addition of skimmed milk to the diet (1½ c.cm. per 10 pounds body-weight weekly). Analysis of the tables showed that it had little influence in hastening retrogression of lesions in the early neural cases, but the experiment is not yet sufficiently advanced for conclusions to be drawn. A further interesting observation made is that children who receive the maximum dose of *Hydnocarpus* oil appear to improve more rapidly than those on lower doses.

*Mambalam village survey.*—A survey of the *cheri* (Mambalam village) is described in detail in the report which shows that while the gross incidence of leprosy is only one-fifth of that in Saidapet proper, every definite case was shown to have had contact with an

open case of leprosy; for instance when a case of neural leprosy was discovered, somewhere near to his hut an open case would almost invariably be found. Indeed the distribution, of leprosy seemed to centre round five foci of infection, of whom three were alive and two dead. Six cases were traced to the three existing open cases, and 14 to the two deceased ones. Another feature was that the majority of cases were traceable to extra-familial sources of infection, largely because, for purposes of contact, the whole village may be taken as a single family group, whereas in Saidapet proper caste distinctions are more in evidence and so contact is mainly intra-familial. Lastly the evidence was all against the poor dietetic condition of the *cheri* predisposing to more widespread infection or resulting in a more serious type of leprosy.

#### *Tuberculosis*

The report contains an abstract of the tuberculosis survey and this reveals a most disquieting situation. Of 638 persons examined, 446 showed no physical signs of tuberculosis, but of the remainder, 186 required further examination; of these, 126 had physical signs in the lungs and were x-rayed, as were also 114 who showed a strong Mantoux but no physical signs of tuberculosis. In passing it may be said that 67.8 per cent of the adult population of Saidapet reacted positively to the Mantoux test and 41 per cent of children (under 12)—both high rates. The latter figure points to a serious home or school source of infection which should be urgently investigated. In all, 33 individuals were found to be suffering, without any doubt, from active tuberculosis requiring treatment. In addition 107 others required further observation and possibly treatment, because of physical and x-ray findings, and 54 of these were children under 12.

As in leprosy, the infection rate is much higher in those living in contact with open cases, and as a corollary, it was evident that overcrowding was a more serious factor than purely a poor economic condition. The tuberculosis mortality rate works out at 462 per 100,000 of the population; the corresponding figure in England is only 76 per 100,000 and the Saidapet numbers must all unfortunately be regarded as minimum figures. A survey has still to be made into the causes of the high tuberculosis infection, morbidity and mortality rates in Saidapet, and it is gratifying to know that a start is to be made later this year, in tackling the problems of further investigation and treatment.

#### *Social*

The report also contains an account of the social work carried out by the students of the Y. M. C. A. College of Physical Education, for it was early realized that the work to be carried on outside the clinic in the homes and streets would be almost as important as that of the laboratory. It has already been indicated how the initial fears of failing in the house to house survey proved to be groundless, and this is largely because of the way in which suspicion has been disarmed, through the school play programme and the maternity centre, etc.

The remainder of the report deals with the economic and sociological survey, and gives an outline of the future programme, which aims at the accumulation of further valuable statistics concerning the general health level of the children, in order that the right steps may be taken to raise that level. It ends with a complete clinical record of one child and is liberally illustrated with photographs, plans and tables.

There is a concluding note which reminds the reader that the results cannot but be secured slowly, for although the work is amongst individual cases, the information in the final analysis is concerned not with the individual cases only, but with the problem of how to control and eradicate leprosy and tuberculosis in a given district. Great satisfaction lies in the quiet revelations of the report that the research work of the association is acting as a lever to elevate the health level of the entire community, and thus it merits the interest and support of all progressive men and women.

### ANNUAL REPORT ON THE WORKING OF HOSPITALS AND DISPENSARIES IN THE PUNJAB, FOR THE YEAR 1938

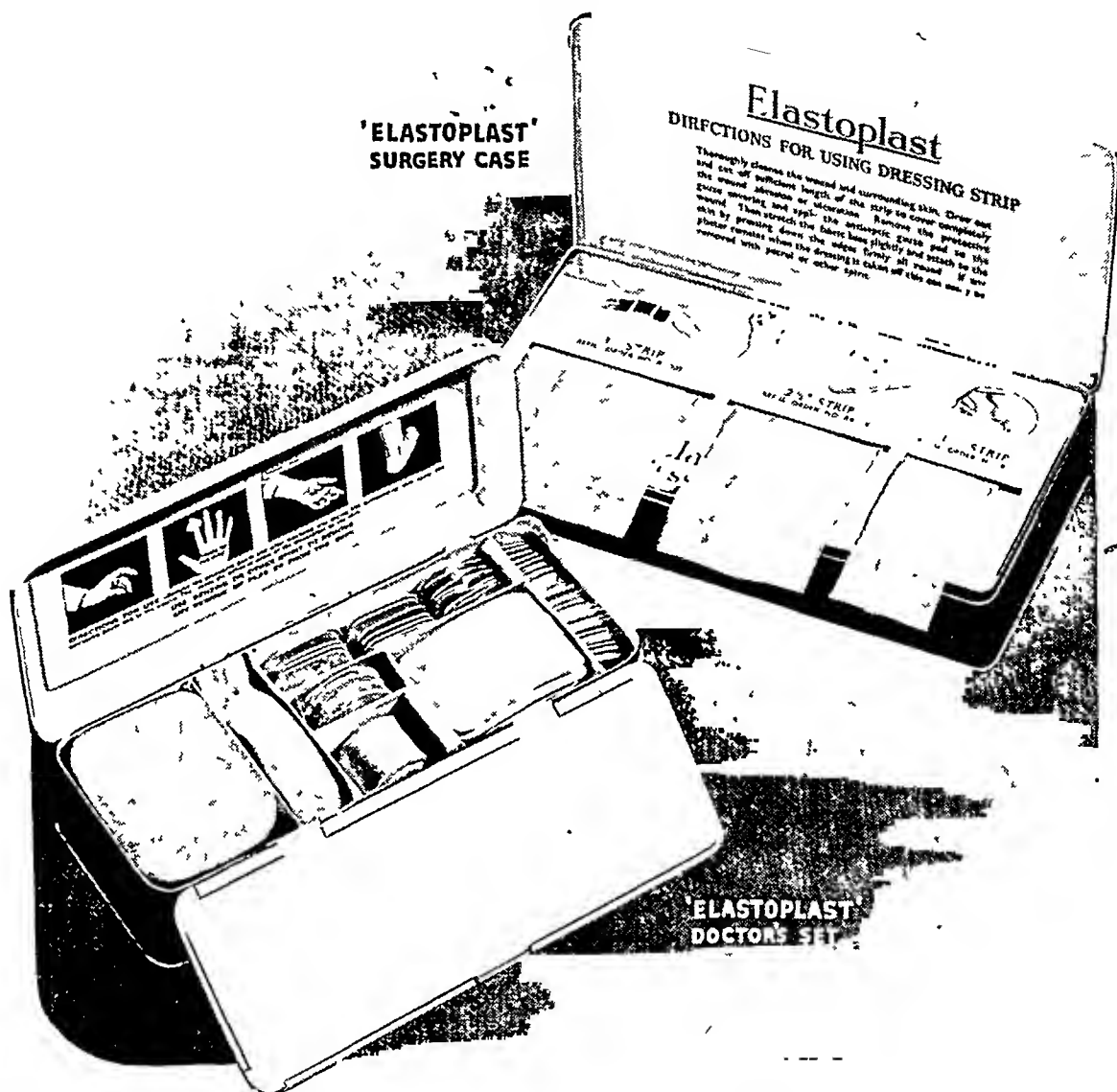
DURING the year under report the total number of medical institutions was 974 (697 in rural areas and 277 in urban areas) against 968 in the preceding year. Two canal dispensaries were closed, but five more were opened in connection with the Haveli Project. The hospitals at Jhelum, Jhang-Mughiana, Batala and Rajanpur and the hospital for women at Beri in the Rohtak district were provincialized. The number of rural dispensaries remained the same, namely, 364; but their sphere of usefulness was widened. The scheme requiring medical officers in charge of these institutions to visit neighbouring villages within a radius of five miles on payment of a fixed travelling allowance of Rs. 10 per mensem which was introduced in 1937, was extended to ten other districts. In order to bring medical relief within easy reach of the rural population at a minimum cost to the exchequer and also with a view to encouraging the spirit of self-help, Government have given a new orientation to their policy. They have now embarked on a scheme of subsidizing private practitioners who will be encouraged to settle in villages with the promise of a subsidy of Rs. 1,200 per annum, half of which will be paid by Government and the other half by the villages themselves through co-operative societies or other similar collective organizations. The experiment was started recently and has been received with enthusiasm in several places.

The total number of patients treated both indoor and outdoor was 171 lacs against 162 lacs in the preceding year. The increase is most noticeable in the case of patients suffering from diseases of the eye and is an indication of the popularity of eye centres, where mainly cataract operations are performed. The phenomenal increase in the number of cholera patients from 139 to 4,251 is due to the importation of infection by pilgrims returning from the Kumbh fair at Hardwar. There was a decrease in the number of patients treated for malaria, which is attributable not only to the disease being less prevalent, but also to a growing tendency amongst the people to treat themselves with quinine without resorting to hospitals.

The total expenditure on hospitals and dispensaries maintained by Government or local bodies or by private organizations with a grant-in-aid by Government was Rs. 52.38 lacs against Rs. 51.18 lacs in the previous year, the principal increase being under the head 'Establishment' on account of the annual increments of the staff. The increase in expenditure on medicines and diet was due to the treatment of a larger number of patients. The income from fees and voluntary contributions rose from Rs. 2.62 lacs to Rs. 2.96 lacs. It appears that patients who can afford to pay for medical treatment are beginning to realize that any payment made by them will help to extend the facilities for medical relief to those who are too poor to pay. The Inspector-General of Civil Hospitals is not satisfied that local bodies are fully alive to the necessity of the proper maintenance of the institutions under their control. Government realize that unless a local body is able to raise additional funds by fresh taxation or from some other source, it is not in a position to expand its activities. But they trust that the standard which has already been attained as a result of several years' effort will not be allowed to fall.

Considerable attention was paid during the year under report to the supply of medical aid to women by members of their own sex. The female hospital at Beri in the Rohtak district which was constructed through the generosity of a public-spirited philanthropist, and the women's sections attached to the civil hospitals at Campbellpur and Jhang-Mughiana were provincialized. The hospitals for women at Bhakkar and Sirsa in charge of municipal committees which had been closed down were reopened. The number of beds available for women increased by 115, of which 59 were in women's hospitals. A sum of Rs. 60,000 was provided





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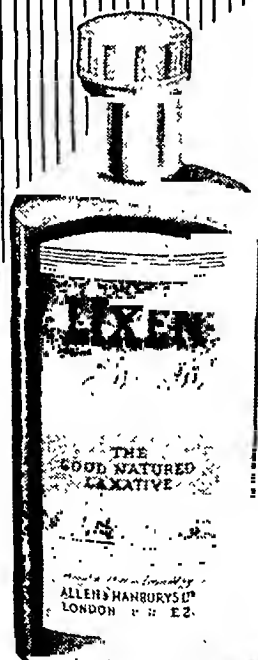
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from the Government of India grant for rural construction to be spent on scholarships to encourage women from rural areas to be trained as *dais* and nurse-*dais*.

Government have still before them the ideal that there should be a separate hospital for women at the headquarters of each district and a separate female section in charge of a woman sub-assistant surgeon attached to each *tahsil* headquarters hospital. But the achievement of this ideal is still remote, for financial reasons. The other limiting factor was the insufficient supply of Punjabi women doctors. Now, however, this is not likely to present any serious difficulties, as medical education among girls is becoming increasingly popular. During the year under report there were 108 Punjabi women students studying for the M.B., B.S. degree and 209 were undergoing a training to qualify themselves as sub-assistant surgeons.

The principal institutions maintained by Government, namely, the Mayo Hospital, the Lady Willingdon Hospital, the Lady Aitchison Hospital, and the Dental Hospital at Lahore and the Civil Hospital, Amritsar, retained their usual high standard of efficiency. A new x-ray plant was installed at the Mayo Hospital at a cost of more than Rs. 1 lac. The construction of a Radium Institute in connection with the hospital has been made possible by the munificence of L. Tirath Ram who gave a generous donation of Rs. 50,000. A whole-time clinical pathologist was appointed at the Civil Hospital, Amritsar. The Lady Aitchison Hospital was so popular that there was a daily average attendance of 99.65 indoor patients for 100 beds and notwithstanding overcrowding admission had to be refused in many cases. The number of ante-natal cases at the Lady Willingdon Hospital increased from 203 to 306 and of surgical operations from 1,169 to 1,567.

A conference of civil surgeons was held at Lahore in April 1938, under the chairmanship of the Inspector-General of Civil Hospitals. The idea was well conceived and the conference proved a great success. Apart from providing an opportunity for establishing personal contacts, the deliberations of the conference resulted in important suggestions for economy and improvement in medical administration. Another noteworthy event of the year was the appointment of a committee to consider whether steps should be taken to provide for the registration of practitioners of the indigenous systems of medicine and whether anything could be done to secure better education in these systems.

#### ANNUAL REPORT OF THE MALARIA ADVISORY BOARD, FEDERATED MALAY STATES, FOR THE YEAR 1939. BY A. NEAVE KINGSBURY, CHAIRMAN

##### *An example of unsuccessful plasmoquine prophylaxis*

ALTHOUGH plasmoquine was introduced twelve years ago there is still no unanimity on its value in field prophylaxis. Under laboratory or hospital conditions the drug is a powerful gametocide, but attempts to utilize its gametocidal action for the control of malaria in the field have given very variable results. A renewed attempt to define the prophylactic value of the drug under plantation conditions was made by the Malaria Research Division, Institute for Medical Research, during 1938 and the early months of 1939.

In describing this experiment to the board, the senior malaria research officer stated that the plantation selected was one on which gametocidal prophylaxis might fairly have been expected to operate under conditions favourable to success. It was well isolated from outside sources of infection, both human and anopheline, while the population of about 700 men, women and children was under such control that the regular administration of the drug could be assured.

Prophylaxis started in March 1938, and continued for one year. The plasmoquine was given under personal supervision at a dosage of 0.02 gm. twice a week for adults and proportionately less for children. Control was regarded as unsatisfactory. The incidence of clinical malaria remained high, while many *P. vivax*

gametocyte carriers were found at routine blood surveys. There was, moreover, strong circumstantial evidence of continued transmission of infection, for wild-caught mosquitoes were found occasionally to be infected and most of the children born on the estate during the year developed malaria within a few months of birth. Two out of every three new-comers, the majority arriving without evidence of existing malaria, developed one or more attacks during the year. Most of the fresh infections that were observed during the period of prophylaxis were with *P. vivax*, but some fresh *P. falciparum* infections undoubtedly occurred.

At first, experimental attempts to infect mosquitoes from *P. vivax* gametocyte carriers known to have received plasmoquine regularly, were mostly unsuccessful: a few gut infections were obtained but no infections of the salivary glands. Later, however, gland infections were obtained. It appears that the discordant results reported in connection with plasmoquine prophylaxis may possibly be explicable by specific differences in response by *P. vivax* and *P. falciparum* to prophylactic dosage.

Dr. I. G. Cameron remarked that contradictory results were published as a result of investigations made on estates near Kuala Lumpur in 1928-29. (Then, the dosage of plasmoquine was twice that used in the present experiment, and now generally recommended for prophylaxis). Dr. B. Barrowman stated that when he was in charge of the estate where Dr. Field's experiments were carried out, and the population was under eighty, he had found that quinine and plasmoquine successfully controlled malaria but such effective control was not obtained whenever the population rose above approximately that number. The population was now 700 and the infection rate, despite prophylaxis, was 14 per cent per month. He considered that the possibility of control of malaria with drugs depended on the size of the population to be protected. He had observed that all reports of the failure of plasmoquine to control malaria had been where the numbers treated were large, while reports of success with the drug had been when the numbers treated were small, and he suggested that all experiments should be scrutinized with this point in mind. The senior malaria research officer pointed out that when, on the same estate, about 400 people were under observation, of whom one-third were subjected to atebirin prophylaxis, the results were regarded as highly satisfactory despite the presence of a large parasite reservoir in a comparable control group.

##### *Attempted prophylaxis with 'M.3'*

An Italian drug known as 'M.3', prepared by the State Biochemical Institute in Milan, has recently been introduced into Malaya. 'M.3' contains mercury and manganese as a double iodide combined with spleen extract and is said to be a valuable prophylactic against malaria. It is claimed that the drug stimulates immunity, improves anaemia and reduces the size of the spleen: administration in rising doses on alternate days for a month is said to confer an immunity which, in the tropics, lasts for six months. It is further claimed that the preparation is a better preventive of malaria than is quinine.

A test sample was recently supplied to the Institute for Medical Research by the courtesy of the local distributors. The senior malaria research officer reported that three hundred adults who had little malarial immunity and were exposed to fairly heavy transmission had been selected for observation; 100 were receiving a full course of 'M.3'; 100 were receiving 1.0 gm. of quinine sulphate weekly; and 100 were untreated controls.

There was little evidence at the end of the year, i.e., after 2½ months' treatment, of any significant reduction of malaria in the 'M.3' group, but a longer period of observation is necessary before definite conclusions can be drawn.

In addition to this brief account of drug prophylaxis the report contains a large amount of information which is mainly of local interest, nevertheless it might be read with advantage by those interested in malaria

control elsewhere, because they are sure to find many items that will be applicable to their own problems.—  
EDITOR, I. M. G.]

## ANNUAL REPORT OF THE MYSORE STATE MEDICAL DEPARTMENT, FOR THE YEAR 1938

THERE were 311 medical institutions working in the State at the close of the year 1938 against 291 at the end of the previous year.

Of the 311 institutions, 279 are classed as public, 26 as non-public (jail, military, forest, railway, etc.), and six as private-aided institutions. There are 32 maternity hospitals and female dispensaries exclusively for the use of women and children.

Including 13,078 parturition cases treated in the various hospitals and dispensaries 61,537 new in-patients were admitted during the year as against 53,251 in the previous year, showing an increase of 8,286 in the current year, i.e., an increase of 15.5 per cent.

During the year 5,612,993 new out-patients were treated as against 5,271,437 in the previous year. Of these 3,485,302 were adults and 2,127,691 children. 4,293,342 were Hindus, 1,060,174 Muslims and 259,477 others; 4,124,665 attended personally and 1,488,328 were represented by friends or relatives. The daily average number of out-patients treated was 25,663.84 against 26,256.91 in the preceding year.

A total number of 335 midwives were working during the year compared with 325 in the preceding year.

A total of 32,038 parturition cases were conducted during the year both in and outside the medical institutions against 30,355 in the previous year. Out of these 13,078 were done in institutions and 19,010 outside.

As in the previous year there were 32 maternity hospitals and female dispensaries. A total of 881 beds was provided in these institutions for the use of in-patients including parturition cases, against 772 in the preceding year.

## Correspondence

### OBSERVATIONS ON THE USE OF NICOTINIC ACID IN THE TREATMENT OF PELLAGRA AND ALLIED CONDITIONS

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—In the May number of the *Indian Medical Gazette*, Dr. W. R. Aykroyd has criticized my statement that 'pellagra is quite common in Bengal'.

According to Sen Gupta *et al.* (1939), the Calcutta School of Tropical Medicine treats six to twelve cases of pellagra per annum. I myself have seen classical pellagra in parts of Bengal as far apart as Chittagong and Midnapore, and more recently in Calcutta.

I admit that in my experience advanced cases of classical pellagra are not common, but I believe that mild cases of pellagra and especially cases which respond well to nicotinic acid are quite common.

The truth of the matter is probably best expressed by Napier (1939) who wrote as follows 'If medical officers in India were more familiar with the signs and symptoms of pellagra it is probable that far more cases would be diagnosed'.

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Yours, etc.,

J. GOODALL,  
CAPTAIN, I.M.S.

Second Resident Medical Officer.

PRESIDENCY GENERAL HOSPITAL,  
CALCUTTA.

24th May, 1940.

## BRITISH PHARMACEUTICAL PRODUCTS

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—Our attention has been drawn to the article on 'British pharmaceutical products' commencing on page 175 of your issue of March 1940, and the two tables which appear on the following pages.

The article is apparently an extract from a publication which appeared in England very shortly after the outbreak of war, which contains a certain amount of misleading information, a certain amount of information which is untrue so far as India is concerned, and which takes no note of developments that have occurred since the outbreak of war.

The items in which we are interested are as follows:—

**Knoll products**—The following Knoll products appear in the tables under the heading 'Foreign Product':—

Bromural	Iod. calcium diuretin
Calcium diuretin	Matronax (known in India as
Cardiazol	Klimakton).
Digipuratum	Styptol
Diuretin	Styracol
Euresol	Tannalbin

The position with regard to Knoll products is, that the trade-mark rights in the United Kingdom are owned by Messrs. Knoll, Limited, London, an English firm closely affiliated with Messrs. Savory and Moore Ltd., and immediately after the outbreak of war, arrangements were made to carry on the manufacture of these in England, and at the present time they are definitely English products, manufactured and marketed by an English company. Arrangements have been made for the English company to supply the requirements of India, and continuity of supply to India of these particular preparations is now assured.

**Argyrol**—This is given as a 'Foreign Product', but this is not correct so far as India is concerned.

For many years the requirements of India have been supplied by the Canadian factory, and Argyrol, in so far as this country is concerned, is definitely an Empire product.

**Veganin (Warner)**—This is starred as a 'Foreign Product' now manufactured in England.

So far as India is concerned, this has never been a foreign product. All supplies made to India since the first introduction of Veganin, have been manufactured in England, and this is definitely an English product.

We shall esteem it a favour if you will take any measures possible to correct any misleading impressions that may arise from the publication of this article.

Yours, etc.,

MESSRS. MARTIN AND HARRIS,  
LIMITED.

MERCANTILE BUILDINGS,  
LALL BAZAR,  
CALCUTTA,  
29th May, 1940.

## Service Notes

### APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL W. H. HAMILTON, C.B., C.I.E., C.B.E., D.S.O., K.H.P., to be Director of Medical Services in India. Dated 12th March, 1940.

The Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's personal staff:—

To be Honorary Surgeon

Colonel D. F. Murphy, M.C., vice Colonel A. C. Munro, vacated. Dated 22nd October, 1939.

The services of Colonel D. H. Rai, M.C., have been placed at the disposal of the Government of the C. P. and Berar, with effect from 11th March, 1940, and he has been granted leave from 11th March, 1940, to 14th May, 1940, preparatory to retirement.



## HEADACHE IS DISABLING

Headache may be as disabling as a grave illness. In migraine particularly, the headache is of all degrees of intensity, at times so severe as completely to incapacitate the sufferer. It is noteworthy how quickly the patient can obtain relief with Veganin. Composed of minimum doses of acetylsalicylic acid, phenacetin and codeine, Veganin affords striking proof of the superior analgesic potency of this synergistic alliance over that of its components administered separately. Recurrent painful conditions, such as migraine and dysmenorrhœa, yield with impressive promptness to the efficacy of Veganin.

**VEGANIN** TABLETS

Supplied in tubes of 10 and 20. Veganin is not advertised to the public.

*A trial supply to Physicians on request.*

**MARTIN & HARRIS LTD.,** Mercantile Buildings, Lall Bazar, Calcutta.

Also at Bombay, Madras, Karachi and Rangoon.

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the satisfactory results. Many patients have been seen after operation, enjoying excellent health and highly satisfied with the result.

Further objections have been raised against subtotal gastrectomy in this country on account of the bulkiness of the Indian diet, but no fears need be entertained on this account. Another objection to the ulcer-exclusion operation, recently referred to by Lahey and Marshall (1939), is possible difficulty of drainage of the pyloric stump if stenosis is present at the site of the ulcer or if it develops later. I do not perform the operation in the presence of stenosis, and have not seen or heard of any after-effects of this kind.

As there is no reason as yet to suppose that the acid levels of Indian stomachs differ considerably from the European, the discrepancy in the results is not easy to explain. Recently Rokitsky's neurogenic theory of the origin of peptic ulcer has been revived and there is experimental evidence in animals that division of the vagus nerves results in considerable lowering of gastric acidity. It is possible therefore that in ligation of the blood vessels in the region of the cardia, these nerves are included. Wilson Hey has claimed that ligation of a large number of the gastric vessels is followed by lowering of gastric acidity, and this claim has been supported by Somervell (1940) among others. It is difficult to understand the mechanism by which this is brought about, for in the ulcer-exclusion type of gastrectomy an equal number of vessels is ligatured or divided. Wells (1939) has suggested that the results of vessel ligation might be due to inclusion of branches of the vagus in the ligatures, and I am inclined to agree with this suggestion. Moreover, in the operation which I practise, little of the pyloric antrum is left. This also may be an explanation of the satisfactory results.

In my opinion, the majority of cases, as seen to-day in India, are such that an ulcer-exclusion type of operation is all that can be done with safety. For those who consider or find the post-operative recurrence of a high acid level to be a danger, the original operation may be regarded as a *first stage* procedure, the pyloric stump being removed at a *second stage* operation some weeks or even months later.

#### *Management and technique*

*Pre-operative technique.*—Each patient is subjected to a careful general examination, special attention being paid to the state of the blood and to a search for intestinal parasites of which the most important is the hookworm. Every one of these patients shows some degree of anæmia. It is often very severe and many patients are admitted with a hæmoglobin percentage as low as 40. Such cases obviously require energetic anti-anæmic treatment to improve this state of affairs. A possible factor in the causation of this anæmia is the chronic gastritis from which nearly all these cases seem

to suffer. Stomach washes, iron, vitamin B, and injections of liver extract are our most potent remedies in the improvement of the anæmia in all cases, with in addition a course of appropriate anthelmintics where intestinal parasites such as the hookworm or the roundworm are found. Hookworm infestation is found to be very common and requires eradication before operative treatment can be proceeded with. The intravenous injection of large doses of Neohepatex (Evans) has been found a most valuable remedy in bringing about rapid improvement in the more severe cases of anæmia and has in fact proved life-saving in cases of acute anæmia following one or more severe hæmatemesis. Its effect is especially valuable for it is usually impossible in this part of India to secure donors for blood transfusion. Anæmia is the most serious complication with which we have to deal, for it has far-reaching effects on all the vital organs, and it is not inconceivable that some of the damage resulting from it is irreparable. We find it safe however to operate on all cases once the hæmoglobin percentage has risen to 70 per cent.

The teeth and mouths of practically all patients require attention, and in many gross caries and infection are present. It is very difficult, however, to persuade patients to submit to routine dental extraction and their reluctance to part with extremely carious and filthy teeth is truly amazing. The infection is often so bad that it is possible that the extraction of such teeth may actually have a deleterious effect in flooding the system with organisms to which the mouth and possibly the stomach have long become accustomed. We have to content ourselves usually with cleaning the mouth by frequent mouth washes during the period of treatment. No serious results, so far as the operation itself is concerned, have been observed through following this very conservative dental regime.

The diet given during the pre-operative period is the ordinary Indian hospital diet consisting mainly of rice, bread, country vegetables, potatoes, plantains, buttermilk and milk, with the usual flavouring ingredients. The diet contains approximately 71 gm. of protein, 20 gm. of fat and 560 gm. of carbohydrate with a caloric value of 2,780. It really requires fine clinical judgment to determine when the patient is fit for operation and this is the most difficult task of the pre-operative period. On it will depend the success of the operation.

*Operative technique.*—Spinal anæsthesia is used in all these cases. Of the many spinal anæsthetics on the market, I have found Percaine, Ciba (1 in 1,500 solution), to be the most suitable for all forms of upper abdominal surgery, and in an experience of some 5,000 spinal anæsthesias with this drug I have seen only two cases to which a fatal termination could be attributed to the drug. It fulfils especially all the requirements



of gastric surgery as it produces perfect relaxation and is sufficiently lasting to enable the operation to be concluded in comfort, both to the patient and the surgeon. The fall in blood pressure which always occurs with spinal anaesthesia is very rarely of sufficient severity to cause anxiety. A dosage of 10 to 11 c.c.m. has been found sufficient for Indian patients and while the majority experience nausea at some stage of the handling of the stomach this very soon passes off. The anaesthetic is administered according to the Howard Jones technique with the head of the table lowered 10 to 15 degrees, and with the patient curled up on his side. The dura is entered with a fine short-bevelled spinal needle between the 3rd and the 4th lumbar vertebrae or in some cases between the 2nd and 3rd. The injection is given slowly and the patient is turned over on to his face immediately after its completion. After 5 minutes in the prone position he is turned over on to his back. Not more than a few drops of cerebro-spinal fluid are allowed to escape before the injection is given. Headache following this technique is very rare.

I have found it necessary to stress our preference for spinal anaesthesia, for it is often stated that this type of anaesthesia is unsuitable for gastric surgery, and some even state that it is dangerous. It has not been so in my experience. Lahey and Marshall (*loc. cit.*) recently stated that, from their experience of Pereaie in upper abdominal surgery, it appeared to be the 'nearly ideal anaesthetic particularly for subtotal gastrectomy'. The patient is given morphia gr.  $\frac{1}{4}$  and scopolamine gr. 1/150 half an hour before operation.

The abdomen is opened by a right upper paramedian incision in all cases, except those in whom a gastro-jejunal ulcer is present, when a midline incision extending from the xiphoid cartilage to the umbilicus is employed. The midline incision in these cases is used mainly to avoid the paramedian incision of the previous operation. The right upper paramedian incision with reflection of the rectus outwards is used because not only can the gastrectomy be satisfactorily concluded through it but the appendix and also the gall bladder, if need be, can be dealt with easily. The appendix is invariably removed and in this country it is remarkable how often it is found diseased. It is nearly always thickened, kinked or adherent, and its removal through a midline incision extending down to the umbilicus or through a left paramedian incision of whatever length would often be difficult and require an undesirable degree of traction, even with the perfect relaxation secured by spinal anaesthesia. The gall bladder usually appears healthy but in a small proportion of cases it is obviously diseased and contains stones. Its removal is left as the last stage of the operation, and it is excised only if it is felt that the patient's condition will permit it. Patients

stand the gastrectomy so well that it has usually been found possible to remove the gall bladder when indicated.

Once the abdomen is opened the ulcer (almost invariably duodenal) is carefully examined. The neighbouring duodenum and the stomach are inspected and palpated in turn and the type of operation decided upon. The gall bladder, pancreas and liver next receive attention and after them the intestines. Finally, the appendix is delivered and excised.

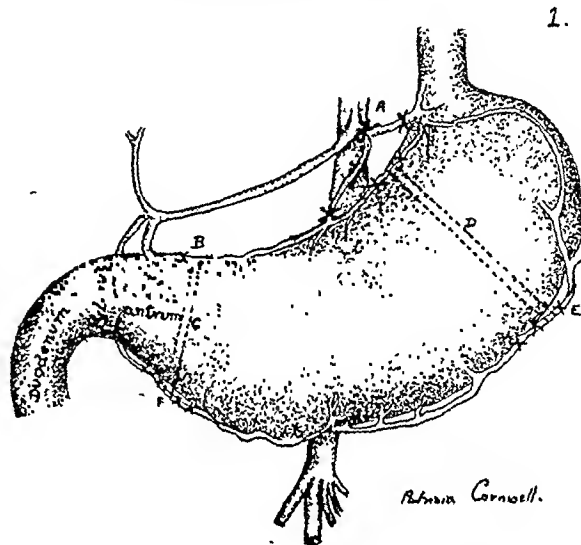


Fig. 1.—Posterior view of stomach showing:—  
 A. Site of left gastric artery.  
 B. Site of right gastric vessels.  
 C. Site of distal division of stomach between the row of clips.  
 D. Site of proximal division of stomach.  
 E. Site of ligature of left gastro-epiploic vessels.  
 F. Site of ligature of right gastro-epiploic vessels.

The details of the operation are as follows:—The stomach and the transverse colon are delivered into the wound and the site of distal gastric section (figure 1) is selected 3 fingers' breadth proximal to the pylorus and marked by the application of a pair of Allis forceps to the greater and lesser curvatures, respectively. The gastro-colic omentum is put on the stretch and opened at an avascular portion. The stomach is drawn over to the right and the left gastro-epiploic artery is secured and divided between artery forceps. Proceeding from left to right, the gastro-colic omentum is further divided between artery forceps for a sufficient length to enable easy examination of the posterior wall of the stomach. The region of the pyloric antrum and pylorus is almost invariably slightly adherent to the serous covering of the pancreas and to the mesocolon, from which however it can usually be stripped readily with a sweep of dry gauze. The right gastro-epiploic artery is then clearly demonstrated and divided between forceps. We consider that unless the operation is proceeded with in this fashion ligation of the right gastro-epiploic artery is likely, on occasion, to endanger the middle colic artery or one of its

branches. The remainder of the gastro-colic omentum is similarly dealt with. At this stage all the divided vessels are ligatured. A feature of the operation, as described by Ogilvie, is the division and ligature of the vessels between the gastro-epiploic arch and the stomach. This I have given up, for these vessels are often so short that the ligature has to be tied almost on the main artery or so close to it as to introduce the possibility of converting the epiploic arch into a thrombosed cord. I have had, furthermore, an opportunity on two subsequent occasions of observing the omentum after the right and left gastro-epiploic vessels had been tied, and the conversion of the omentum into a fat-graft productive of adhesions, as predicted by Ogilvie, had not occurred. The vessels along the greater curvature having been divided the stomach is then drawn down and an opening is made in the gastro-hepatic omentum with the fingers. Of the leash of vessels which go to

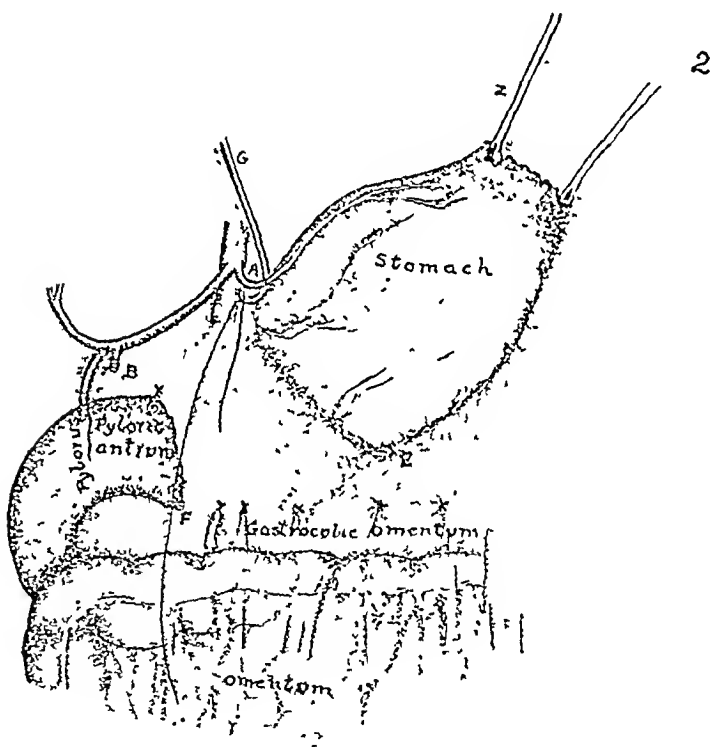


Fig. 2.—The stomach has been turned up over the left margin of the abdominal wound and the aneurism needle (G) has been passed under the left gastric artery (A) close to its origin. The vessel is double ligatured at this site. The pyloric antrum has been doubly oversewn with 00 catgut.

supply the region of the pylorus and the first part of the duodenum one turns to the left, and it is secured near the point at which the stomach is to be divided. The Friedrich-Petz sewing machine is now applied and the stomach is divided with scissors between the double row of clips. The distal stump comprising the pyloric antrum is then doubly oversewn with 00 catgut.

The remainder of the stomach is then turned upwards and over the left margin of the wound so as to define the commencement of the left gastric artery, which has to be further

exposed by a little gauze dissection. When exposed it is underrun with an aneurism needle, double ligatured and divided (figure 2). This manoeuvre of high ligation of the left gastric artery, as pointed out by Ogilvie, greatly mobilizes the stomach and is considered essential for the better functioning of the proximal gastric stump. Before proceeding further with the resection numerous large vessels, which reach the stomach in the region of the cardia from the left gastric artery, require ligation at this stage. These vessels are particularly numerous on the posterior wall of the stomach. The site of proximal division of the stomach is then selected and marked by the application of Allis forceps. The line of division at the lesser curvature should be within  $1\frac{1}{2}$  inches of the cardia, and the line of division at the greater curvature should be above the site where the left gastro-epiploic artery reaches the stomach. The line of gastric section therefore lies almost at a right angle to the lesser curvature at the site of section. A long straight-bladed clamp is then applied to the stomach. I have had made for me a pair of clamps for application to the stomach and jejunum which hold lightly and do not crush. To avoid any possibility of the stomach receding out of the clamp a pair of Allis forceps are applied to the lesser and greater curvatures, respectively, just proximal to its site of application. The jejunum is then brought up so that the proximal loop joins the lesser curvature (figure 3). The jejunum is brought either through (retro-colic anastomosis) or in front of the mesocolon (ante-colic anastomosis) depending on the length of the mesocolon. In the latter case, a slightly longer loop is necessary. Considerable care must be taken in determining the length of the proximal loop and allowance must be made for the fact that once the anastomosis is complete and the stomach released it retracts back high up under the costal margin. The length of the loop which we find sufficient is that which reaches easily to the surface of the abdominal wound without any stretch whatever being applied to it. If the anastomosis is of the retro-colic variety the left leaf of the incised mesocolon is at this stage sutured to the under surface of the stomach proximal to the clamp. If the anastomosis is carried out with the proximal jejunal loop at the greater curvature (only two cases in the series) the length of loop required is somewhat less than that required for the more usual operation. The stoma is in all cases placed at the greater curvature and is always made sufficiently large to admit four fingers.

The seromuscular suture is commenced at the lesser curvature (figure 3) and is of the continuous Dupuytren type. When it reaches the greater curvature it is locked and held. The Petz clamp is applied and the stomach resected with scissors between the rows of clips. A sufficient number of clips is then

cut out to provide an adequate stoma, a few clips (in practice usually five) being left at the lesser curvature to form a spur. The jejunum is opened to a corresponding length. The hæmostatic layer is commenced at the greater curvature and is a simple running suture, six to the inch, and locked at every fourth stitch (figures 4 and 5). It turns at the lower end of the spur and is continued along the anterior wall of the stomach to end at the greater curvature where it is tied. In order to prevent undue pouthing of the gastric and jejunal mucosa, the stitch, which is passed from jejunal to gastric side, picks up a slightly lesser bite of jejunal and

If the anastomosis has been retro-colic the right leaf of the opening in the mesocolon is now affixed to the stomach with five or six interrupted catgut sutures. Figure 7 shows the completed ante-colic anastomosis.

I have used the Friedrich-Petz sewing machine for nearly all gastrectomy operations for over two years, and consider that it adds an element of safety to these operations. The suture line is absolutely water-tight. The machine, however, has to be used with discretion in cases of hypertrophied stomachs and, in my opinion, it is better not to use it at all in such cases. Such a state of affairs hardly exists in

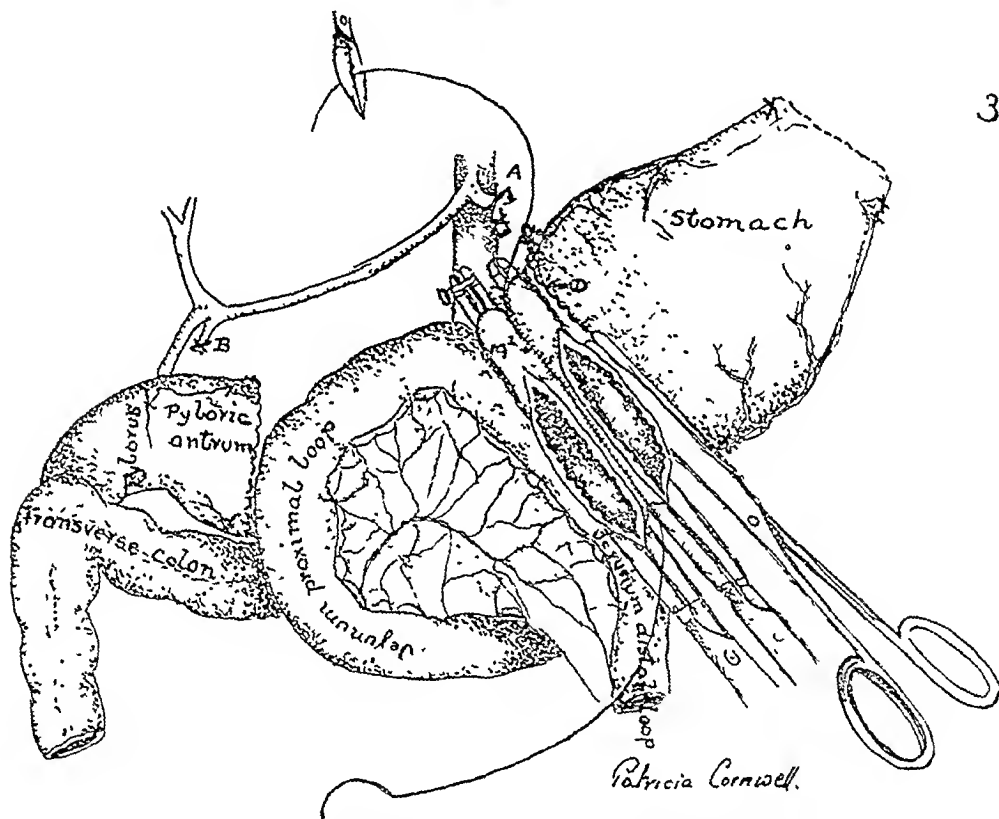


Fig 3—The jejunum has been brought up with the proximal loop to the lesser curvature of the stomach. The clamps have been applied and the first seromuscular layer of sutures (M') commenced at the lesser curvature has been completed. The stomach is being cut away with scissors and the clips cut out at the site of the stoma. Five clips are left to form a spur at the lesser curvature. (In practice the stomach is cut away first and then the appropriate number of clips are cut out.) The jejunum has been opened.

gastric mucosa than it does of jejunal and gastric seromuscular coats

At this stage the clamp on the jejunum is removed. The seromuscular suture, which had commenced at the lesser curvature and was locked and held at the greater curvature, is then brought along the anterior surface of the stomach and jejunum and ends at the lesser curvature. The remaining clips forming the gastric spur are enfolded by jejunum only and are not oversewn separately and buried in the gastric wall (figure 6). 40-day catgut (00) is used for the seromuscular and 20-day catgut (00) for the hæmostatic layer of sutures.

the type of duodenal ulcer for which we perform gastrectomy, but it does sometimes exist in cases of gastro-jejunal ulcer, and also in stomachs at the site of a gastric ulcer situated close to the pylorus. In these instances, of course, an ulcer-exclusion type of gastrectomy would not always be done.

*Post-operative technique.*—The patient on return to the ward is given immediately 4 ounces of glucose water by mouth, one pint of coffee rectally, and after this continuous rectal saline is commenced and maintained for 48 hours. The Fowler position is adopted after 4 hours.

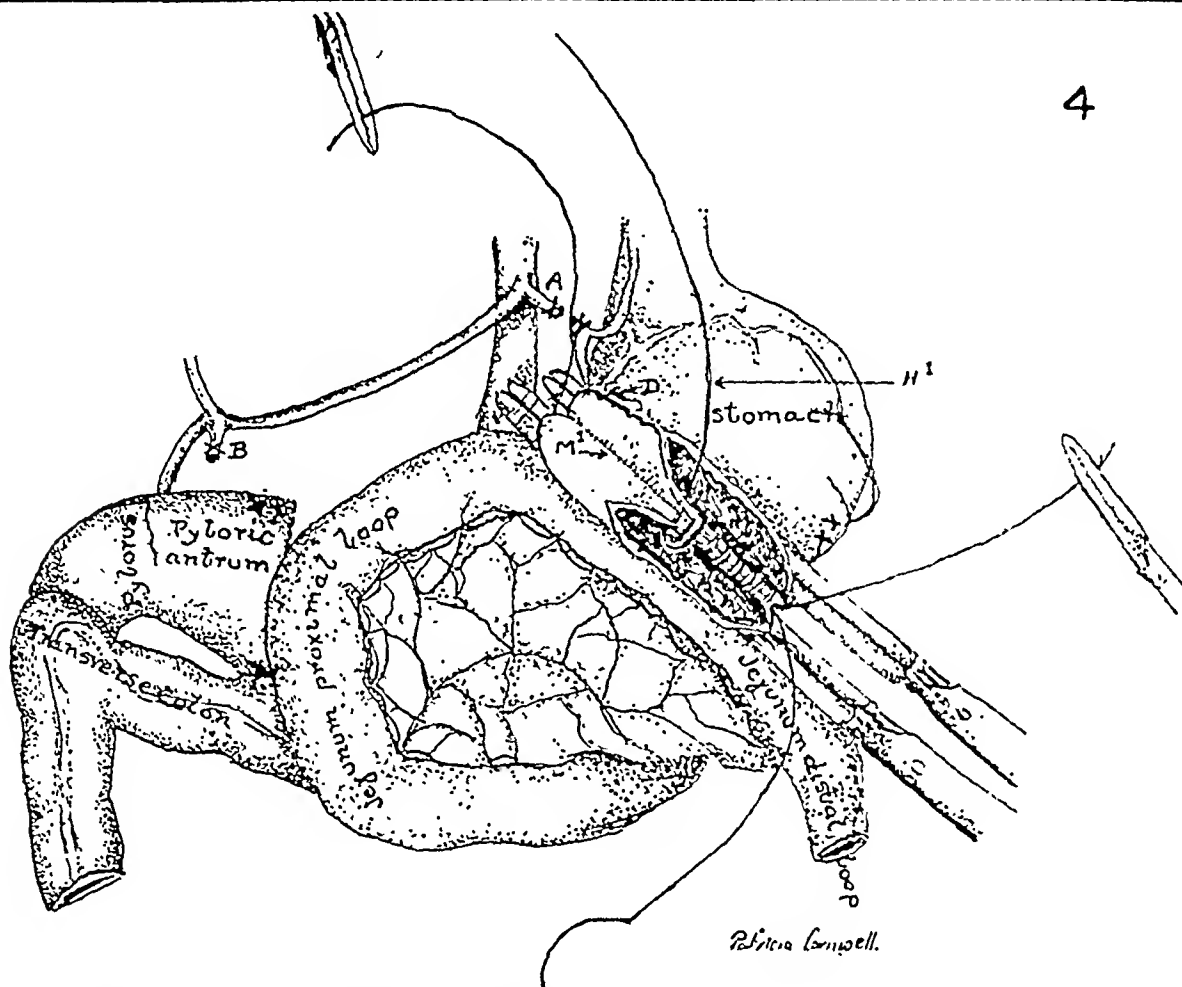


Fig. 4.—The layer of hæmostatic sutures has been commenced at the greater curvature.

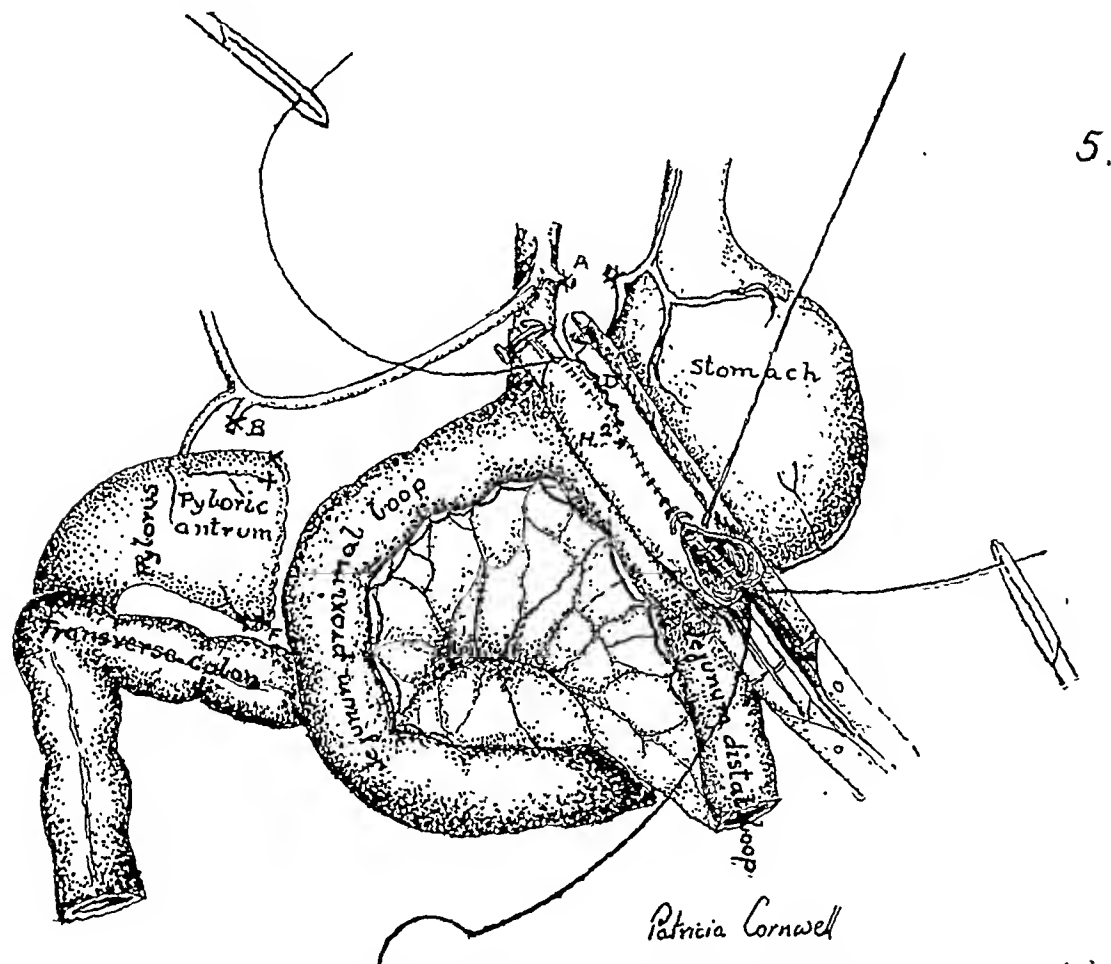


Fig. 5.—The hæmostatic layer is returning to the greater curvature where it will be tied. It is a simple over and over suture locked at every fourth stitch.

Food by mouth is given in accordance with the following scheme :—

- 1st day .. If the patient is very thirsty, one ounce of hot glucose water is given occasionally throughout the day in addition to the above.
- 2nd day .. One ounce glucose water by mouth every two hours. Continuous drip rectal saline is continued throughout the day.

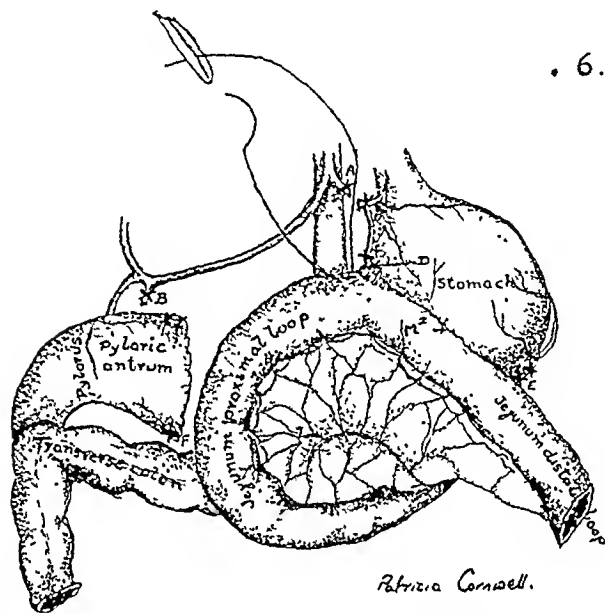


Fig. 6.—The anterior seromuscular layer of sutures (M') is nearing completion and the spur is being oversewn and buried in jejunal wall. The suture on completion is tied at the lesser curvature. In practice the stomach is not released from the clamp (not shown in the diagram) until the layer of sutures is nearing its completion.

- 3rd day .. Albumin water sweetened with glucose is given, two ounces every three hours. Rectal saline is occasionally continued as on first and second days.
- 4th day .. Whey and albumin water sweetened with glucose, two ounces every two hours.
- 5th day .. Citrated milk diluted with equal parts of water, four ounces every three hours.
- 6th day .. Whole citrated milk, four ounces every four hours. Strained orange juice.
- 7th day .. Milk (with coffee to flavour), six ounces every four hours. Strained orange juice if desired.
- 8th day .. Whole milk, six ounces every four hours, with egg-flips. Strained orange juice if desired.
- 9th day .. As above, plus two biscuits and three ounces of bread.
- 10th day .. Add eight biscuits.
- 11th day .. Eight ounces of bread given.
- 12th to 14th day. Convalescent milk and bread diet plus extras such as ten ounces of mutton broth, six ounces of rice in buttermilk, two eggs, cod-liver oil twice or thrice daily.
- 15th to 17th day. Rice eight ounces, and vegetable curry four ounces for the day. Patient is allowed out of bed on the 15th day.
- 18th and 19th day. Ordinary Indian diet.
- 20th day .. Patient discharged from hospital.

The pulse rate is closely watched throughout the first 48 hours and any sudden increase of 10 beats or more per minute, especially if accompanied by profuse sweating, is taken as an indication for the immediate passage of a duodenal tube (Ryle's, Jutte's or Wagensteen's). This is only occasionally necessary and the tube is not passed as a routine. Once passed, however, it is left in for 48 hours and connected to a Cathcart drip apparatus. Reference has previously been made to the state of the mouths of these patients, and to overcome the very real danger of post-operative parotitis a slice of lime is given to the patient to suck every 3 hours, and both parotid glands are gently massaged by the nurse in charge every 4 hours. Frequent mouth washes of dilute potassium permanganate solution are given throughout the convalescence. Since adopting this regime acute post-operative parotitis has not occurred. Each patient wears a pneumonia jacket and is turned frequently from side to side throughout the first few days of the convalescence. If broncho-pneumonia develops, an expectorant mixture containing ammonium carbonate is

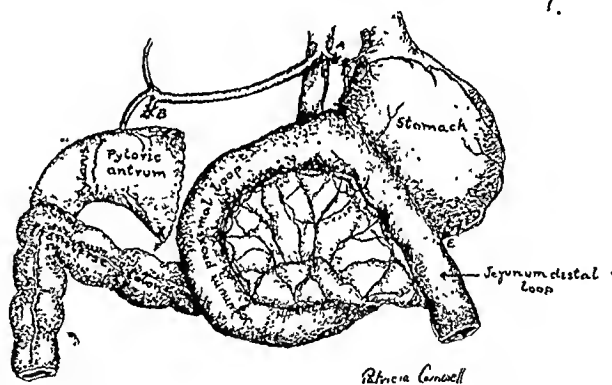


Fig. 7.—The operation has been completed. The stomach when released from the clamp passes high up and to the left under the costal margin. The proximal jejunal loop is diagrammatic in all the drawings. In practice it is shorter and passes more directly upwards and to the left.

given every 4 hours, and at the same time injections of vitamin C are given in large doses twice daily. This has proved a particularly valuable remedy in the treatment of post-operative pneumonia.

# RESULTS.

*Immediate results.*—170 cases of duodenal ulcer have been subjected to this operation. There have been 10 deaths giving a mortality rate of 5.9 per cent.

Causation of death	Number of cases
Hyperpyrexia .. .. .	3
Spinal anaesthesia .. .. .	1
Post-operative tetanus .. .. .	1
Hæmatemesis .. .. .	1
Broncho-pneumonia .. .. .	4

Hyperpyrexia occurred in 3 cases operated on during very hot weather, and is to be avoided by refraining from the performance of such operations during the period of the year when the temperature is highest.

The death which we attribute to the spinal anaesthetic followed a comparatively easy operation. The pulse rate on return to the ward was 80 per minute and of good volume. After an hour it began to rise steadily and continued increasing until the evening, when death occurred. The patient was quiet, was not sweating and remained conscious until the end. There were none of the usual signs of shock or internal hæmorrhage. It was not possible to examine the heart and lungs after death, but the abdomen was opened and the field of operation was found to be normal. This death is attributed to the anaesthetic in the absence of any other obvious reason, because an exactly similar death had occurred after another operation, and because several cases during the same period had developed similar symptoms but had fortunately recovered.

The death due to post-operative tetanus occurred in a patient operated on 16 days before, whose convalescence had otherwise been quiet and uneventful. Extensive investigation failed to reveal the source of infection.

The mortality rate of 5.9 per cent in this series of cases is admittedly high, but causes of death such as hyperpyrexia, anaesthesia and tetanus might be regarded as regrettable accidents and to be avoided in a further series.

The convalescence is usually uneventful, and not only has there been an actual gain in weight but the anaemia also has improved in all the cases operated on. It is this improvement in anaemia that leads me to believe that the anaemia, from which the patients nearly always suffer on admission, is nutritional and the result of long-standing gastritis. The operation is tolerated well by patients of all ages, the oldest in the series being just under 80 years of age and the youngest 18 years.

*Late results.*—It is not easy to determine with accuracy the later results. All cases are invited to return to hospital for re-examination after 3 months and at later intervals. Many avail themselves of this invitation and have appeared well, with a few rare exceptions. We have not been able to see all the cases operated on but have sometimes been able to trace patients by adopting the practice of questioning every new patient admitted to hospital for chronic peptic ulcer, as to whether there are any other cases in his village treated by us for a similar complaint. It is surprising how much we are able to learn in this fashion about our old cases. One case has returned with gastro-jejunal ulceration and three cases, all of whom were found to be suffering from heavy hook-worm infection, have returned on account of severe secondary anaemia. We are satisfied

(Continued at foot of next column)

## REPORT OF PNEUMONIA ENQUIRY AT THE MAYO HOSPITAL, LAHORE, DURING THE YEARS 1938, 1939 AND 1940

By GEOFFREY F. TAYLOR, M.A., M.R.C.P. (Lond.)  
MAJOR, I.M.S.

Professor of Clinical Medicine, King Edward Medical College, Lahore

and

NAND LAL CHITKARA, M.B., B.S.

IN 1938, the Punjab Government gave a grant for the investigation of pneumonia in the Mayo Hospital, Lahore. The grant was exhausted by the end of March 1940, and this report gives the results obtained.

Earlier reports of results at the Mayo Hospital by Chand *et al.* (1939) and Taylor and Chitkara (1939) have been published and a further paper on 'Pneumococcal Lung Abscess' has been submitted recently to the *Lancet* for publication.

The work done includes typing of the pneumococci obtained from pneumonia cases, clinical investigation, treatment by new drugs, particularly M. & B. '693' ('Dagenan') and Felton's concentrated anti-pneumococcal sera, and investigation of other pneumococcal infections associated with pneumonia, particularly pneumococcal meningitis, empyema, lung abscess and pericarditis.

The cases recorded are the usual type of admissions to the Mayo Hospital, Lahore, mainly Indian, Punjabi Muslims, Hindus and

(Continued from previous column)

that in Indian patients at any rate, the operation is not productive of a high rate of gastro-jejunal ulceration and that it is preferable to a gastro-enterostomy, in the absence of stenosis. We have observed also that the operation in no way lessens the ability of the patient to earn his living by hard manual labour if necessary and that it permits him to enjoy his usual diet in comfort.

My thanks are due to my assistant Dr. C. S. S. Sarma for the very great help he has given me in the preparation of this paper, and to Miss Patricia Cornwell for her excellent semi-diagrammatic drawings. I have also to thank Major-General N. M. Wilson, C.I.E., O.B.E., K.H.S., I.M.S., Surgeon-General with the Government of Madras, for permission to publish the paper.

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Sikhs, with a few Europeans and Anglo-Indians. They are mainly of the poorer classes admitted to the general wards of the hospital.

Seventeen cases were admitted to the hospital in a moribund condition during the period and died within twenty-four hours from the time of admission, usually within a few hours. These cases are not included in this report.

### I. Typing of pneumococci

Two methods were used, Neufeld's 'Quellung' method and agglutination by type sera. The typing sera used for Neufeld's methods were obtained from Parke, Davis & Co., using

thirty different type sera and six mixtures. The technique employed was that described in Parke Davis's pamphlet with a slight modification which will be reported later. Thirty different types of sera for the agglutination method were kindly sent to us by the Public Health Department of New York, free of charge. As far as possible both methods were used in each case.

A full report of the work done on typing is being prepared and will be published later.

The following is a summary of the results of typing pneumococci from pneumonia cases :—

Total cases typed—196.

TABLE I

Type																Mixed	Mixed	Mixed	Indeterminate type
1	2	3	4	5	6	7	8	10	11	12	13	15	20	21	25	1 and 2	7 and 9	11 and 13	
74	14	7	1	1	3	12	5	1	2	3	2	3	3	1	1	5	1	2	55

TABLE II

The number of cases of each type of pneumococci found each month

Year 1939	Type														Indeter- minate type
	1	2	3	4	5	6	7	8	11	12	15	20	Mixed 1 and 2		
January ..	9	1	1	..	..	1	3	..	..	..	..	..	..	1	
February ..	17	1	1	..	..	..	3	..	..	1	..	..	..	13	
March ..	6	..	1	..	..	..	..	..	..	..	..	..	1	5	
April ..	15	2	..	..	..	..	1	..	..	..	..	..	1	3	
May ..	9	2	2	..	..	..	1	..	..	..	..	..	1	7	
June ..	2	1	..	..	..	..	1	..	..	..	..	..	1	12	
July ..	2	1	..	..	..	..	..	..	..	..	..	..	2	5	
August ..	1	..	2	..	..	..	..	..	..	..	..	..	..	..	
September ..	1	..	..	..	..	..	..	..	..	..	..	..	..	2	
October ..	2	..	..	..	..	..	1	2	..	..	..	..	..	1	
November ..	2	..	..	..	..	..	1	..	..	..	..	..	..	..	
December ..	3	2	..	1	..	1	1	1	1	1	1	1	..	..	

Year 1940	Type																Mixed 7 and 9	Mixed 11 and 13	Indeter- minate type
	1	2	5	6	7	8	10	11	12	13	15	20	21	25					
January ..	2	1	1	1	1	2	1	1	1	2	1	1	1	.	1				
February ..	1	3	..	..	..	..	..	..	..	..	1	1	..	1	..	..	..		
March ..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..		

TABLE III

Relation of pneumonia with age groups and number of deaths

Age in years ..	..	0-5	6-10	11-20	21-30	31-40	41-50	51-60	61-70
Number of cases	..	21	9	84	112	51	21	5	2
Total deaths ..	..	1	0	2	9	11	2	0	1

TABLE IV

*The incidence of pneumonia by months in cases at the Mayo Hospital, Lahore, during the last six years*

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1934 ..	33	46	46	24	21	34	26	21	13	17	48	62
1935 ..	35	22	26	12	29	23	15	4	6	14	18	20
1936 ..	26	26	15	19	28	21	8	14	7	13	13	23
1937 ..	25	16	8	13	12	17	8	7	10	16	30	32
1938 ..	29	20	22	16	30	10	14	6	8	12	33	44
1939 ..	40	38	13	17	23	22	12	3	3	11	12	30

It is seen that type 1 pneumococci are responsible for 37.7 per cent of the total cases.

*Note.*—(1) In the cases shown as 'mixed type', pneumococci of two different types were obtained from a single case indicating infection with two different types of pneumococci.

(2) In the 'indeterminate types' no definite agglutination was found using the sera and no 'Quellung Reaction' occurred. The inability to type about 20 per cent of pneumococci from pneumonia cases by Neufeld's method has been noted by other workers elsewhere. In this work at Lahore it was found also that approximately 20 per cent of cases could not be typed by the agglutination method.

(3) Twenty cases showed positive agglutination results with type sera, but showed no 'Quellung Reaction' using Neufeld's method.

No typing was done during the months of November and December 1938, as the necessary sera were not available.

The small number of cases of type 1 pneumococci in January and February 1940 is striking when compared with the same months of 1939.

Further work is needed for a number of years to determine the changes in the types of pneumococci occurring during different years and different months of the same year. Unfortunately no funds are now available to do this.

## II. Some details of interest noted in the clinical manifestations of the cases during this period

Out of 305 cases of pneumonia admitted during the period 1938-40, only nine cases showed an insidious onset. The remainder had an acute onset.

The diagnosis of pneumonia was made either by the physical signs of frank consolidation, or when the physical signs were not definite, by x-ray confirmation of consolidation. Mild cases of 'pneumonitis' were excluded from this series.

The highest incidence of pneumonia is thus between eleven and thirty years of age, between which ages 65 per cent of the cases occurred.

The high incidence during the winter months of November to February is probably due to the low temperature which often touches freezing

point. The cause of the rise of the incidence in May and June is not so obvious as these are the hot dry months with the maximum temperature up to about 110°F.

Twenty-one of the 305 cases which form the material for this report had broncho-pneumonia, the remaining cases being of the lobar type.

TABLE V  
*The lobes involved and their number*

Mono-lobular	Poly-lobular	LEFT LUNG		RIGHT LUNG		
		L. L. lobe	L. U. lobe	R. L. lobe	R. M. lobe	R. U. lobe
139	145	159	53	167	67	51

The lower lobes were more commonly involved, the right lower lobe slightly more frequently than the left.

TABLE VI  
*The leucocyte count on admission, and details of the differential count*

	0-5,000	5-10,000	10-20,000	20-30,000	30-40,000
Number of cases.	11	66	148	54	5

Polymorphonuclear count

	0-60%	61-70%	71-80%	81-90%	91-100%
Number of cases.	7	16	70	130	45

The majority of the cases showed a leucocyte count between 10,000 to 12,000 per c.mm.

Enough data are not available to come to any definite conclusion, but as far as they go the types of pneumococci appear to bear no relation to the age of the patient.

There appears to be no relationship between the type of pneumococci and the site or extent of the pneumonia.

TABLE VII

Number of cases of each type of pneumococci isolated from different age groups

Age in years	Type												Mixed	Mixed	Indeterminate group
	1	2	3	6	7	8	10	11	12	13	15	20	1 and 2	7 and 9	
0-10	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3
11-20	23	..	1	1	3	2	1	..	..	..	..	..	2	..	18
21-30	25	7	2	1	5	3	..	1	2	2	..	1	..	..	14
31-40	11	1	..	..	2	..	..	..	1	..	1	..	..	1	8
41-50	5	..	1	..	..	..	..	..	..	..	..	..	1	..	2
51-60	2	2	..	..	..	..	..	..	..	..	..	..	..	..	..

TABLE VIII

The types of pneumococci isolated from cases involving various lobes

Lobes involved	Type												Mixed	Mixed	Indeterminate type
	1	2	3	6	7	8	10	11	12	13	15	20	1 and 2	7 and 9	
Monolobular	..	39	6	2	1	4	..	1	..	2	1	1	3	..	21
Polylobular	..	27	4	3	1	6	5	..	1	1	1	..	..	1	18
Left L. lobe	..	37	6	2	..	3	3	1	..	1	..	..	2	..	20
" U. "	..	9	..	..	..	1	..	..	..	..	..	..	..	..	6
Right L. "	..	41	5	4	2	9	4	..	1	2	1	1	..	..	23
" M. "	..	13	2	..	1	3	3	..	1	1	2	..	..	1	5
" U. "	..	11	2	2	1	..	3	..	1	1	..	..	1	1	3

TABLE IX

Types of pneumococci isolated and the leucocyte count

White cell count	Type												Mixed	Mixed	Indeterminate group
	1	2	3	6	7	8	10	11	12	13	15	20	1 and 2	7 and 9	
0-5,000	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
5-10,000	17	1	2	..	2	1	..	..	2	..	..	1	..	..	6
10-20,000	37	7	3	..	6	4	1	..	1	1	1	..	2	..	21
20-30,000	10	2	..	1	1	1	..	1	..	1	..	..	..	1	10
30-40,000	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..

TABLE X

Types of pneumococci and percentage of polymorphonuclears in the blood count

Percentage of polymorph.	Type												Mixed	Mixed	Indeterminate group
	1	2	3	6	7	8	10	11	12	13	15	20	1 and 2	7 and 9	
0-60	..	..	..	..	..	..	..	..	1	..	..	..	1	..	..
61-70	1	..	..	..	..	..	..	..	..	..	..	..	..	..	2
71-80	28	2	1	..	4	2	..	..	1	1	1	1	..	..	11
81-90	38	8	2	1	5	3	1	..	1	..	..	..	1	1	21
91-100	6	1	1	..	..	2	..	1	..	1	..	..	1	..	4

TABLE XI

*The types of pneumococci isolated and naked-eye appearances of sputum of the cases*

Character of sputum	Type												Mixed	Mixed	Indeterminate group
	1	2	3	6	7	8	10	11	12	13	15	20	1 and 2	7 and 9	
Rusty ..	42	6	2	2	7	5	..	1	2	1	1	..	3	..	10
Tenacious	18	3	1	..	2	1	..	..	..	1	..	..	..	..	18
Mucoid ..	13	4	1	..	3	..	..	..	..	..	..	..	..	1	17
Viscid .	15	..	2	1	6	..	..	..	1	..	..	..	3	1	6
Frank blood	1	1	..	..	..	1	1	..	1	..	..	1	..	..	..
Frothy ..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..

Again the above two tables do not show any obvious relationship of the type of pneumococci to the height of the leucocyte count or to the extent of polymorphonuclear leucocytosis.

Rusty sputum is most commonly found in type 1, but other than this, there appears to be no relation between the type of pneumococci isolated and the character of the sputum.

It appears from the above data that the type of pneumococci isolated from a case of pneumonia bears no relation to the age of the patient, to the number of lobes involved or character of the sputum.

The data shown in the following tables were collected from cases dying of pneumonia :—

TABLE XII

*Leucocyte counts on admission to hospital*

	0-5,000	5-10,000	10-20,000	20-30,000	30-40,000
Number of cases.	1	7	11	5	2

TABLE XIII

*Polymorphonuclear percentage in differential count on admission*

	61-70	71-80	81-90	91-100
Number of cases.	3	10	7	6

From the figures given above, it is concluded that leucopænia and a low percentage of polymorphonuclear leucocytes did not occur commonly in cases of pneumonia which died. Text-books state that a low white cell count is of bad prognosis. Our figures do not bear this out, as they do not differ markedly from those obtained in cases which lived.

TABLE XIV

*Complications recorded in the 305 cases*

Delirium	..	24
Enlarged spleen (malarial)	..	21
Cases unresolved	..	13
Wassermann reaction positive	..	11
'Creeping type'	..	10
Abdominal distension	..	8
Unconsciousness and stuporose condition	..	7
Heart complications	..	5
Jaundice	..	5
Meningitis	..	4
Empyema	..	4
Herpes	..	3
Incontinence of urine	..	3
Parotitis	..	2
Liver abnormally enlarged	..	2
Diarrhoea	..	2
Glossitis	..	1
Acute suppurative otitis media	..	1

TOTAL .. 126

It was noted that thirty-seven cases admitted for pneumonia had had a previous attack of pneumonia.

### III. Methods of treatment of pneumonia cases

During this period 305 cases of pneumonia were admitted into the Mayo Hospital, Lahore. The first 100 cases admitted during the autumn and winter of 1938-39 were treated alternately by the older methods, for control purposes, and by M. & B. '693'. The results were reported by Chand *et al.* (1939). By the time these first hundred cases had been treated it was obvious from reports from all parts of the world, and from our own results, that M. & B. '693' greatly reduced the mortality of pneumonia. It was thus decided to treat all cases of pneumonia in the hospital by this drug. Parke, Davis & Co. kindly supplied us with Felton's concentrated serum at half the usual price in order to enable us to treat some cases with M. & B. '693' combined with Felton's serum.

TABLE XV

The mortality of cases treated in the three ways

	Number of cases	Mortality
(1) Control cases treated by older methods other than M. & B. '693' and Felton's serum.	76	14 or 17.4 per cent
(2) Cases treated by M. & B. '693'.	200	12 or 6 "
(3) Cases treated by M. & B. '693' combined with Felton's concentrated anti-pneumococcal serum.	29	Nil

The cases treated by M. & B. '693' and Felton's serum were twenty-seven of type 1 pneumococci and two of type 2.

The dose of M. & B. '693' used was that described by Gainsford and Evans which is four tablets (2 gm.) on admission, four tablets after four hours and then two tablets four hourly for thirty-six hours, followed by one tablet four hourly for a further thirty-six hours. After treating the first fifty cases we decided that the treatment for the first thirty-six hours was sufficient and we stopped giving the one tablet four hourly for the second thirty-six hours. The concentration of M. & B. '693' in the blood after 24 hours' administration of the drug was 2.5 to 6 mgm. per 100 c.c. of blood.

#### Cases treated by M. & B. '693' alone

The temperature fell to normal within twenty-four hours in 140 cases, and within forty-eight

hours in twenty-seven cases. The consolidation remained for several days after the fall of temperature and resolved only slightly more rapidly than cases not treated by the drug. Many cases continued to cough up blood-stained sputum for several days after the fall of temperature. These aspects of the results of M. & B. '693' treatment are now well recognized and described in the literature on the subject.

The average stay in hospital of M. & B. '693' treated cases was three to four days shorter than the cases treated by older methods.

*Note.*—One hundred and six cases treated by M. & B. '693' were not typed, as the necessary sera were not available during part of the time.

TABLE XVII

The age of cases treated by M. & B. '693' and the mortality in each age group

Age	Total cases	Mortality
0-5	19	..
6-10	9	..
11-20	56	1
21-30	70	4
31-40	29	6
41-50	12	1
51-60	4	..
61-70	1	..
TOTAL ..	200	12

The dose given up to one year of age was one-fourth of the adult dose, namely, one tablet on admission, one tablet after four hours and thereafter half a tablet four hourly for thirty-six hours.

TABLE XVI

The number of each type treated by M. & B. '693' and the mortality in each type

Type	Total number of cases	Mortality	Age groups					
			0-10	11-20	21-30	31-40	41-50	51-60
1	25	1	..	7	9	4	3	2
2	7	..	..	..	5	1	..	1
3	3	..	..	1	1	..	1	..
6	1	..	..	1	..	..	..	..
7	6	..	..	2	2	2	..	..
8	5	..	..	2	3	..	..	..
10	1	..	..	1	..	..	..	..
11	1	..	..	..	1	..	..	..
12	2	..	..	..	2	..	..	..
13	2	1	..	..	2	..	..	..
15	1	..	..	..	2	..	..	..
20	1	..	..	..	1	1	..	..
Mixed 1 and 2	3	..	..	2	..	..	1	..
Mixed 7 and 9	1	..	..	..	..	1	..	..
Indeterminate	35	2	2	17	9	6	1	..
TOTAL ..	94	4	2	33	35	15	6	3

The dose over one year of age up to ten years of age was usually half the adult dosage.

Children tolerated M. & B. '693' well and vomiting occurred in only one case in the age group 0-10, in which twenty-eight children were treated.

It is also remarkable that no death occurred in children up to the age of ten who have been treated by M. & B. '693' during the period of this investigation. Twelve of these children had broncho-pneumonia and the remaining eighteen had lobar pneumonia. Mortality figures of pneumonia in children of the Punjab are not available, but in our experience it was high before the introduction of this new drug.

#### IV. *Complication in cases treated by M. & B. '693'*

The following complications were noted in the M. & B. '693' treated cases :—

1. *Vomiting*.—This occurred in fifty-two cases of the two hundred treated by M. & B. '693'. The drug had to be discontinued because of vomiting in nine cases. In the remaining cases the drug was continued in spite of the vomiting. We tried giving sodium bicarbonate, bismuth carbonate, luminal, and glucose with the M. & B. '693' when vomiting occurred, but these drugs appeared to have no influence on the vomiting and no influence on the pneumonia. In most of the cases, vomiting passed off after the first few doses had been given and it appears that the vomiting will stop in most cases, if the drug is continued.

It has been stated that vomiting resulting from M. & B. '693' is due to the action of the drug on the central nervous system. We found that the vomiting stopped when we substituted injections for oral M. & B. '693', and we consider, therefore, that it is due to the local action of M. & B. '693' on the gastro-intestinal tract. Although the vomiting is extremely unpleasant for the patient it seems to have no deleterious influence on the course of the disease.

2. *Leucopenia*.—White cell counts were done in all cases at frequent intervals. In three cases of pneumonia treated by M. & B. '693', a sharp fall in the leucocytes developed but there were no adverse clinical signs. The patients made uninterrupted recoveries. The original counts were 25,000, 25,000, 20,625 and they fell to 6,000, 6,875, and 6,240. Severe agranulocytosis developed in one case of empyema treated with M. & B. '693'.

3. *Unresolved pneumonia*.—This occurred in four of the M. & B. '693' treated cases, which is not higher than its incidence in cases treated by the other methods.

4. *Empyema*.—This occurred in four of our M. & B. '693' treated cases. This incidence of 2 per cent is not higher than the normal incidence of empyema in cases treated in other ways. When M. & B. '693' was first introduced Gainsford and Evans thought that empyema

developed more frequently in cases treated by M. & B. '693' but after treating a larger number they and others have concluded that the incidence of empyema is not increased in pneumonias treated by M. & B. '693'.

5. *Meningitis*.—Pneumococcal meningitis developed in three of our two hundred treated cases.

6. *Hæmaturia*.—Hæmaturia developed in four cases. Hæmaturia and stone formation have been reported from America as a result of M. & B. '693' treatment. Two cases in American literature showed actual stone formation in the kidney, the stone consisting of M. & B. '693'. In three of our cases there was severe hæmaturia. The fourth case showed red blood cells on microscopic examination. The hæmaturia stopped two or three days after stopping the drug. In one of the cases after a rest of one week, as the temperature was maintained, a second course of M. & B. '693' was given, and it again resulted in a severe hæmaturia. Two of the cases were examined radiologically but showed no signs of stone in the kidney. The American report says that M. & B. '693' stones are not opaque to x-ray. As a result of this experience, it is a safe rule to make that the urine should be examined microscopically daily for red blood cells.

7. *Malaria*.—The spleen was enlarged and hard in eighteen cases, probably from chronic malaria. Two of these cases failed to respond in the ordinary way, the temperature remaining high for two or three days longer than the ordinary period of twenty-four or forty-eight hours. Quinine by the mouth and by injections intramuscularly was given with M. & B. '693'. There appears to be no contra-indication to giving quinine and M. & B. '693' together, when indicated.

8. *Epistaxis*.—Epistaxis was noted in two cases. In one case the epistaxis stopped when the drug was stopped and began again when the drug was given again.

9. *Cyanosis*.—Cyanosis developed in two cases.

#### V. *Cases not responding in the ordinary way to M. & B. '693'*

In addition to the twelve deaths in our M. & B. '693' group, a further twenty-one cases did not respond in the usual way by a fall of the temperature in twenty-four or forty-eight hours. We have also tried to analyse the cause of the deaths but there appears to be no obvious common factor. Nineteen of the twenty-one cases which did not respond to the treatment, completely recovered in the hospital, while two were discharged at their own request with signs of unresolved pneumonia and a continuous high temperature. No tubercle bacilli were discovered in the sputum of these cases although we suspected that one, or possibly two cases, were suffering from active tuberculosis. Two



further cases showed signs of unresolved pneumonia and two others a 'creeping type of pneumonia'. The spleen was enlarged in three of these cases. Acute pericarditis, acute toxic delusional insanity and hæmaturia were noted in other cases of this group. Poverty and anæmia were not marked factors in causing a lack of response to treatment.

Of these twenty-one cases sixteen began treatment five or more days after the pneumonia had developed, when complications were possibly beginning. It appears that treatment of pneumonia with full doses of M. & B. '693' in the first two or three days of the disease is important.

In a further twenty-five cases there was a secondary rise in temperature occurring a few days after it had fallen to normal as a result of the first treatment. This secondary rise was treated by a further course of M. & B. '693' which led to a rapid fall of the temperature to normal in all but five cases. In five cases, vomiting prevented full doses of the drug being given. Two of these cases had an anæmia due to ankylostomiasis. The blood counts were 3,500,000 and 3,000,000 and hæmoglobin 60 per cent and 55 per cent (Sahli). One case developed severe bilateral parotitis but eventually recovered. Four cases had enlarged spleens due to chronic malaria.

#### VI. Cases treated by M. & B. '693' combined with Felton's serum

There is experimental evidence in animals that M. & B. '693' combined with anti-pneumococcal concentrated serum is superior to M. & B. '693' alone in the treatment of experimental pneumococcal infections, if the serum is given early in the disease.

In the Mayo Hospital in 1939 and 1940, twenty-nine cases of type 1 and type 2 pneumonia have been treated with combined M. & B. '693' and Felton's concentrated anti-pneumococcal serum. All twenty-nine cases recovered with no severe complications. Twenty-seven cases belong to type 1, and two cases to type 2.

The dosage of M. & B. '693' was the routine one. On admission the pneumococci were typed by Neufeld's method and as soon as either type 1 or 2 were found, the case was tested for sensitivity to the serum by the skin reaction described in Parke Davis's pamphlet consisting of the injection intradermally of 1/10 c.cm., of anti-pneumococci serum which had been diluted 1 in 10 with distilled water. If the sensitivity test was negative, as it was in twenty-four cases, 40,000 units of Felton's concentrated serum were given intravenously at once, the dose being repeated after four hours and a final 20,000 units being given after a further four hours.

Five cases were sensitive to Felton's serum, as shown by a weal and erythema developing at the site of the intradermal injection. These cases were desensitized by giving 1/10 c.cm. Felton's serum, intramuscularly as the initial

dose, and then at intervals of two minutes doses equal to double the preceding dose until the total initial dose of 40,000 units of serum had been given.

Four cases which were not sensitive to the skin serum test developed anaphylactic shock almost immediately after giving the serum, as shown by respiratory embarrassment and erythematous and urticarial skin rashes. Adrenalin was immediately given in these cases and the reaction subsided within one-half to two hours, without any serious consequences.

One case, which had been found to be sensitive to the skin test, was desensitized but developed severe anaphylactic symptoms when he was given the second dose of 40,000 units intravenously four hours after the first dose. He responded quickly to adrenalin.

Obviously, enough cases have not been treated by this method to give evidence of statistical significance, but twenty-nine cases of pneumonia treated with no deaths indicate that this method deserves further trial.

The difficulties in treating cases by this method are that the pneumococci must be typed as early in the disease as possible, and serum given before the fourth or fifth day of the disease. Given later, it is probably of little use. Also the serum is expensive.

Five cases treated with one batch of serum developed marked restlessness, sweating and a slight rise of temperature a few minutes after the first injection was given, this subsided in about half an hour. These symptoms were not noted in the other cases. They appear to have been due to some special effect of that batch of serum. It has been noted by many workers with other sera that different batches give different reactions.

Clinically these twenty-nine cases treated by the combined serum and M. & B. '693' did not differ from cases treated by M. & B. '693' alone, in the rapid fall of the temperature, or in any other features, except for the anaphylactic phenomena noted above.

#### VII. Other pneumococcal infections

1. *Pneumococcal empyema*.—During this period ten cases of pneumococcal empyema were treated in the medical wards. Early in 1939, treatment by M. & B. '693' combined with repeated aspiration of pus from the empyema cavity was tried in an effort to avoid rib resection. Three cases of early pneumococcal empyema were cured in this way. The pus in two of them was not thick and only semi-purulent. Aspiration was needed only once and twice respectively. The third case had thick pus in the chest and aspiration was done fifteen times. A total dose of 85.5 gm. of M. & B. '693' in thirty days was given. Skiagrams of the chest on discharge from the hospital showed a little thickening of the pleura but otherwise normal. We tried this treatment on five other cases in which the pus was already thick, and

continued it for a period up to five weeks. They did not respond so that rib resection was eventually done. In one of these cases agranulocytosis and exfoliative dermatitis developed and the patient died. Fuller details of these cases are given by Taylor and Chitkara (1939).

The conclusion drawn from this limited experience is that when the pus is thin, aspiration combined with treatment by M. & B. '693' is indicated, but when the pus is thick and loculated, prolonged treatment with M. & B. '693' combined with aspiration does not clear the empyema. Operation should be done as soon as the pus is thick and loculated.

There are reports of several cases of severe agranulocytosis in the literature, but this case of exfoliative dermatitis as the result of M. & B. '693' appears to be the second recorded. The first case was reported by Taylor and Chitkara (1939).

2. *Pneumococcal meningitis*.—During this period nineteen cases of pneumococcal meningitis were treated in the medical wards by M. & B. '693' and daily lumbar punctures. Fuller details of seventeen of these cases have been given by the same authors. There are now many reports of recovery from pneumococcal meningitis by this treatment. The mortality in the whole group of cases is thus approximately 85 per cent. Before M. & B. '693' was introduced, these cases invariably ended fatally.

In three cases in whom type 1 pneumococci were isolated from the cerebro-spinal fluid, Felton's concentrated serum was given in addition to the above treatment, but all three cases died.

3. *Lung abscess*.—During this period seven cases of lung abscess were treated by M. & B. '693'. Fuller details of these will be published later. Three of these cases improved dramatically with M. & B. '693' treatment and completely recovered. Two of the cases died and the two remaining cases could not tolerate the drug by the mouth and left the hospital unrelieved of the symptoms and with the signs of lung abscess persisting. Two of the cases which recovered were given M. & B. '693' injections as they could not tolerate the drug by the mouth.

4. *Pneumococcal pericarditis*.—Three cases have been treated. Two of them had large pneumococcal pericardial effusions and one was a case of dry pericarditis. The two cases of effusion are at present in the wards being treated by aspiration of the pericardial sac and short courses of M. & B. '693', repeated at fairly short intervals. The case of dry pericarditis recovered completely and the other two cases are recovering with treatment.

We wish to thank Lieut.-Colonel Amir Chand, I.M.S., Professor of Medicine, Rai Bahadur Dr. Jivan Lal, Professor of Pathology, and Dr. Mohammad Yusuf of the Medical College, Lahore, for their help. Also Parke, Davis & Co.

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## A NEW METHOD FOR THE RELIEF OF PARALYSIS OF THE OPPONENS POLICIS

By MAX SCHECK, M.D. (Austria)  
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ANALYSING the movements of the fingers which make the hand the useful instrument it is, one comes to the conclusion that holding of tools, instruments, etc., is possible by bending the four fingers around the tool, whereas the grasp between the thumb and the fingers is used for all more subtle movements. These finger movements make the hand more valuable and in many cases are the means by which one earns one's livelihood (violinist, artist, skilled workman). The importance laid on the thumb and its opposing power can be estimated from the social laws of countries with workers' compensation. Whereas the loss of one of the fingers counted as below the compensation rate (I refer to the old Austrian law) the loss of the thumb or its opposing function counted as a loss of 20 per cent of earning capacities. This refers to the skilled workmen. It means much more to the musician, the surgeon or the painter.

To make it possible for the disabled hand to return to the usual functions, surgical methods have been devised. All of them have as underlying principle some sort of tendon

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for giving Felton's anti-pneumococcal serum at half the usual price, May & Baker's representatives for giving some of the M. & B. '693' free and Mrs. Bharucha for buying some of the M. & B. '693' used.

### Summary

(1) Results of typing of pneumococci from pneumonia cases at the Mayo Hospital, Lahore, from 1938 to 1940 are given.

(2) Some details of interest in the clinical findings of the cases, particularly in relation to types, are given.

(3) Results are given of treating 200 cases with M. & B. '693'; some combined with Felton's concentrated anti-pneumococcal serum, with no deaths.

(4) Twenty-eight children with pneumonia were treated and all recovered.

(5) Complications of the treatment are discussed.

(6) Results of treatment of cases of pneumococcal empyema, meningitis, lung abscess and pericarditis are given.

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transplantation. Before doing such an operation two questions have to be answered—

(1) Which muscles and tendons of this region are still working?

(2) Will the elimination of the transplanted tendon not lead to disturbance of the functional equilibrium?

The extent to which muscles and tendons are paralysed depends upon the nature and localization of the original disease. Isolated paralysis of the opponens muscle occurs when the small branch coming from the median nerve and emerging from under the volar ligament of the carpus is cut. This may happen when opening a radial bursa for pyogenic infection.

Extensive paralysis of a group of muscles, including the opponens muscle, will be found in lesions to the median nerve. The muscles innervated by the median nerve are divided in two groups, the proximal and the distal group. According to the level where the nerve has been affected, both the groups are involved or only the distal group. The proximal group comprises pronator radii teres, flexor sublimis digitorum, flexor carpi radialis, palmaris longus, flexor profundus digitorum (the radial half), flexor longus pollicis and pronator quadratus muscles. The distal group comprises the abductor pollicis longus, the opponens pollicis, the two outer lumbricales, and flexor pollicis brevis muscle.

Injuries to the nerve in the region of the elbow (fractures, stab wounds, shots) will involve both groups of muscles. In this case only tendons of muscles innervated by the ulnar nerve can be used for transplantation. A modification of Ney's method is to connect the tendon of the extensor pollicis brevis with one part of the split flexor carpi ulnaris tendon. Lexer proposed to use the abductor of the little finger. After separation from the first phalanx of the little finger the tendon is drawn through a subcutaneous canal in the palm and connected with the opponens pollicis.

If an injury to the nerve occurs distal to the departure of the branches for the proximal group only the muscles of the distal group will be paralysed. In this case muscles and tendons can be used belonging to the proximal group. Ney divides the tendon of the extensor pollicis brevis at the level of the wrist joint after exposure by a dorso-lateral incision extending from the wrist joint to the insertion on the first phalanx of the thumb. A second incision is made on the anterior aspect of the wrist and the tendon of the palmaris longus muscle is exposed. The distal ends of both incisions are then connected by a subcutaneous canal. Through this the tendon of the extensor pollicis brevis is drawn and connected with the palmaris longus tendon. Baeyer fixed the tendon of the flexor longus pollicis muscle to the dorsal side of the thumb after having made an S-shaped incision. The tendon is not divided at the place of insertion.

In these cases of injury to the nerve with a well-defined clinical symptomatology and definite loss of function the task of finding a functional substitute is less difficult than in cases where not only a partial or total paralysis of the nerve is encountered but where also the muscles are directly affected and the ulnar nerve is involved. Such conditions are frequently seen in Volkmann's ischæmic contracture, in cases of extensive burns with scar formation or after cellulitis of the forearm. Here a large number of muscles have lost their function and the difficult task of finding a functioning tendon for transplantation, which in the new function will be of more value than in the old one, is put before the surgeon. It is the object of this paper to describe a new method which was used in a case.

In October 1938 a boy was admitted to the P. B. M. M. Hospital, Bikaner. He gave the history of having had a fall from a tree about ten months back. This resulted in a compound fracture of the humerus above the elbow-joint which was reduced and treated by a layman. The wound discharged pus for a long time and ultimately healed. He could not use his hand and came to this hospital. He was operated upon, but since there was no improvement, he was admitted again. On examination an extensive scar in the region of the right elbow was found, also a linear scar in the course of the musculospiral nerve, from the above-mentioned operation. (An end to end suture of the radial nerve was attempted for radial palsy.)

There was considerable wasting of muscles of the forearm. The wrist joint was in a flexed position which could be increased actively and passively. Extension of the wrist and fingers was actively impossible. Flexion of the fingers could be slightly increased by his own muscular action. He could flex the second phalanx of the thumb but it was impossible to oppose it. There was sensory loss typical of paralysis of the median nerve.

*Diagnosis.*—Radial palsy, with paralysis of the distal group of muscles innervated by the median nerve.

The radial palsy was most probably a direct consequence of the injury whereas the lesion of the distal part of the median nerve originated in the resulting suppurative and scar formation. An operation on the radial nerve did not seem worth while, as the suture of it had proved unsuccessful. An exploration of the median nerve was not considered advisable since it is very rare for an operation on the nerve in the region of the forearm to give a good result. Our plan was to reconstruct the opponens function and then to use the flexor carpi ulnaris and radialis muscles for transplantation to the fingers and the thumb respectively. To use the flexor longus pollicis muscle was the idea of the first part of the operation.

On 13th October, 1938, the operation was done under general anaesthesia. Through a vertical incision in the middle of the volar aspect of the thumb extending from the metacarpo-phalangeal joint to the base of the second phalanx the flexor longus pollicis tendon was exposed. It was then divided at its insertion on the second phalanx. The base of the first phalanx was exposed subperiosteally and a hole drilled through it in a dorso-volar direction. The tendon was threaded through and the end stitched to the proximal part by means of silk sutures, after having brought the thumb into the opposed position. A supporting plaster splint was kept on for two weeks. The wound healed by first intention.

Two weeks after operation the boy was encouraged to active movements. Within a week he could bring the tips of thumb, index and middle fingers together. In March 1939 he was re-examined. He could oppose the thumb to the fingers. There was considerable

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## AUTOMATIC FLYPROOF LATRINE SEAT

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BEFORE I come to the actual description of the automatic flyproof latrine seat, a few points about fly-breeding will not be out of place. These points actually drew my attention to the necessity for an automatic device which I think is essential in dealing with the problem. There is a general belief that fly-breeding occurs mainly in manure and rubbish heaps, and consequently efforts are made to stop breeding in such materials rather than in human excreta, which, I consider, is a profuse breeder. This, I have repeatedly demonstrated as follows:—

I take three ordinary jam jars, and fill them up one-third with loose earth. On top of the earth is spread a layer about half an inch thick of human excreta in the first, animal droppings in the second and rubbish in the third. One dozen flies are placed in each of the jars and covered with nettings.

Factors such as the sex of flies, their age and period of fertility were ignored.

The flies are allowed to remain in the jars for twenty-four hours.

The jars are covered again with the netting, and left until the flies have hatched out. The time taken in hatching will depend upon temperature, humidity, etc. It is always observed that the jar containing human faeces contains innumerable flies. In the jar containing animal droppings there are fewer flies, whereas in the jar containing rubbish the number of flies can be easily counted. This experiment may be tried in different seasons but the results are invariably the same. It may be noted that maggots appear faster and in greater profusion if there is ample moisture and food for them in the medium.

The prevalent idea about fly-breeding in manure and rubbish heaps, etc., may be true in cold climates, and in countries better managed from the point of view of sanitation. In these places human excreta is seldom left lying about and, in any case, the climatic conditions are not so conducive to fly-breeding at such a rapid pace. In a tropical country like India, however, human excreta from the time it is voided to its

final disposal affords an admirable medium for fly-breeding, if left exposed.

Experience shows that once human faeces are exposed to flies, and eggs laid on them, no amount of trouble and expense at the trenching ground will prevent the eggs from hatching into flies. My experience in the Jail Department and Cantonments has convinced me of this. In the Jail Department there is no dearth of labour and material for efficient trenching, and yet in spite of all that I could do to prevent fly-breeding in the trenches, I found that a very large number of flies did hatch out. The places from which they came out in large numbers were in between two adjoining trenches. In some places this space was altogether honeycombed. A large number of birds were usually seen in the early morning and late evening near the trenches, evidently come there to feed on the young flies freshly hatched out.

Anti-fly measures in vogue at present in many places are to let flies breed, and then concentrate on ways and means of destroying them by poison, traps, fly sprays, etc. This method of dealing with the fly nuisance is not only very expensive but also inefficient, inasmuch as the flies have done a lot of damage before they are ultimately destroyed, and they have also laid the foundation for thousands of more batches to hatch out later.

In order, therefore, to prevent fly-breeding it is not only the ultimate disposal of excreta that is important but even more so is the protection of excreta from exposure to flies. This exclusion, to be perfect, must begin where the excreta is voided and continued right through to the point of final disposal.

The excreta may be exposed to flies in the following places:—

1. Latrine receptacles.
2. Filth bins.
3. Filth carts, for removal from the bins to its final disposal in trenches or by incineration as the case may be.
4. At the place of ultimate disposal in trenching grounds or in incinerators. The stage where most of the eggs are laid is in the latrine receptacles. Efforts have of late been made in certain places to flyproof group latrines but this is worse than useless for the following reasons:—

(i) The building is provided with a single door, which enables flies to enter and makes their exit difficult, so that in the case of such a flyproof building, the arrangement acts as a trap and the result is worse than if the building had been left freely open.

(ii) As it is a shady place, flies are tempted to get into the building during the heat of the day.

(iii) The wire gauze doors and windows are often damaged and remain unrepaired, and give flies ample opportunities to shelter in the shade inside.

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strength in the grasp and he could hold various objects. The strength of the grasp could be increased by dorsiflexion of the wrist. A third operation the aim of which would have been to relieve the drop wrist by tendon transplantation was refused by the boy. A splint was given for the extension of the wrist joint.

#### Conclusions

(1) A new method is described for the relief of paralysis of the opponens pollicis. The flexor longus pollicis tendon is used for the transplantation.

(2) The result has been satisfactory.

(iv) It is an expensive method because of the upkeep of wire gauze which is often broken by misuse.

I have had opportunities of observing this type of latrine in controlled population day after day and as a rule I found them harbouring more flies than open latrines.

The pan or receptacle into which excreta is passed is the part of the latrine which attracts flies. It contains the 'bait' and it is the fly-proofing of this receptacle which is the important point to aim at. In order to be thoroughly effective and to comply with caste prejudices of Indians the flyproofing of the seat must be automatic in action. It should be so arranged that, without touching it with the hands, it shall open just previous to the act of defæcation and automatically close immediately afterwards. With the object of effecting this, the latrine described below has been devised.

Efforts have been made to devise latrines of the squatting type for Indians where the pan remains closed when not in use and opens up automatically when it is in use. The working parts in some of them are complicated and require constant attention to keep them in good condition. In other cases the latrine seats require some manipulation on the part of the user which may be against caste prejudices, or again this manipulation may be difficult for children, and a nuisance when an individual is in a hurry to use the latrine. In order, therefore, to obviate the above disadvantages, the following latrine has been designed after years of practical experience, use, and repeated experiments. The principal object of the device is to provide a pan which, when not in use, will remain covered. A further object is that the lids of the pan should automatically open when the user occupies the platform and close when the platform is vacated. A third object is to construct a sanitary latrine that can be easily made, cheap in cost, sturdy and simple in design and construction, with a mechanism requiring the minimum amount of care either on the part of the user or the sweeper.

#### *Description of the latrine*

Figures 1 and 3 give the front and side views of the latrine when not in use.

Figures 2 and 4 give the front and side views of the latrine when in use.

In all the figures—

1. The platform supported on legs.
2. The opening in the platform through which excreta and urine drop into the pan when it is uncovered and ready for use.

3. The mobile foot rests, to the undersurface of which are fixed three vertical rods—the central being the working rod, and the two side ones guide rods.

4. The central working rod.

5. The guides.

6. Vertically rotating pulley fixed to the lower end of the working rod. This works on

7. Lever fixed at an angle on the upper surface of

8. The lids.

9. The pan that receives the excreta. This slides in and out for emptying and cleaning purposes. Note that there is no space left between pan and lids and that the pan when being replaced after cleaning cannot be pushed either beyond or on either side of the lids, so that it always remains completely covered.

10. The handle provided for pulling out the pan and pushing it back into place.

11. The pivot on which the lids open and close. The device does away with hinges which are apt to rust. When the seat is not in use as

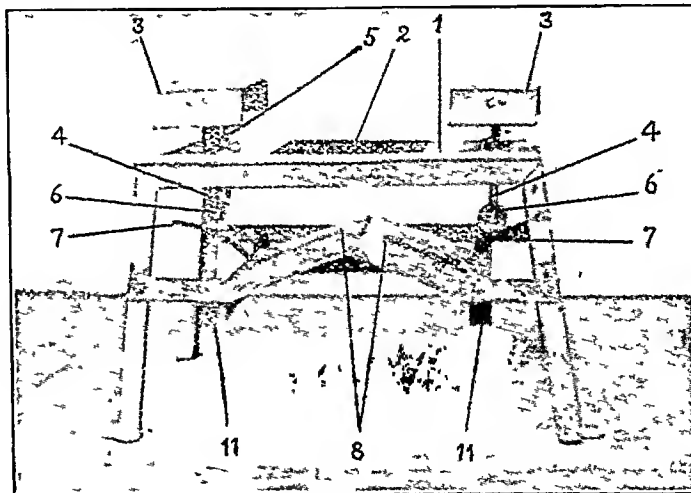


Fig. 1.

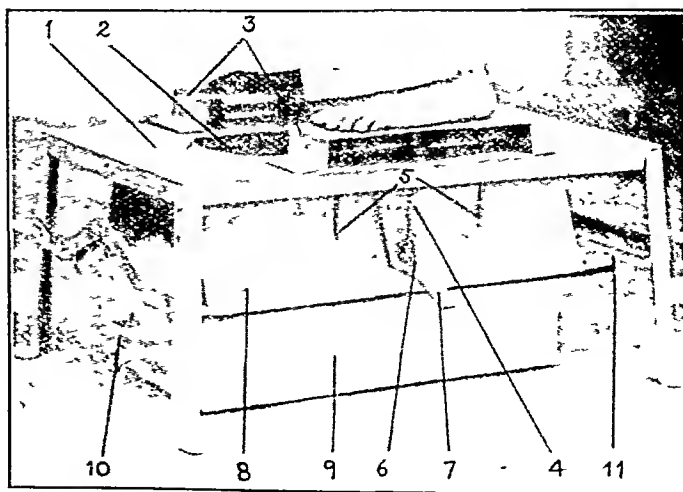


Fig. 2.



in figures 1 and 3 the lids cover the pan so that it is impossible for flies to get in. A point in the construction worth noticing is that the lids do not hermetically seal the pan but loosely cover it, allowing passage for foul air from the pan to the outside air and vice versa. This prevents the stench which is noticed with a commode when once used. A number of persons can thus use this seat one after another, and frequent cleaning of the pan by the sweeper is not necessary. When it is desired to use the seat the user puts his feet on the mobile foot rests which are thus pressed down. Nine pounds of weight is all that is required for this purpose, and therefore a small child can use the seat, if once shown how to do so.

The working rods with the pulley at their lower ends, on being pushed down with the foot rests, act on the levers attached to the lids, and raise them as shown in figures 2 and 4. The pan is thus uncovered and ready for use. The lids when opened are totally covered by the

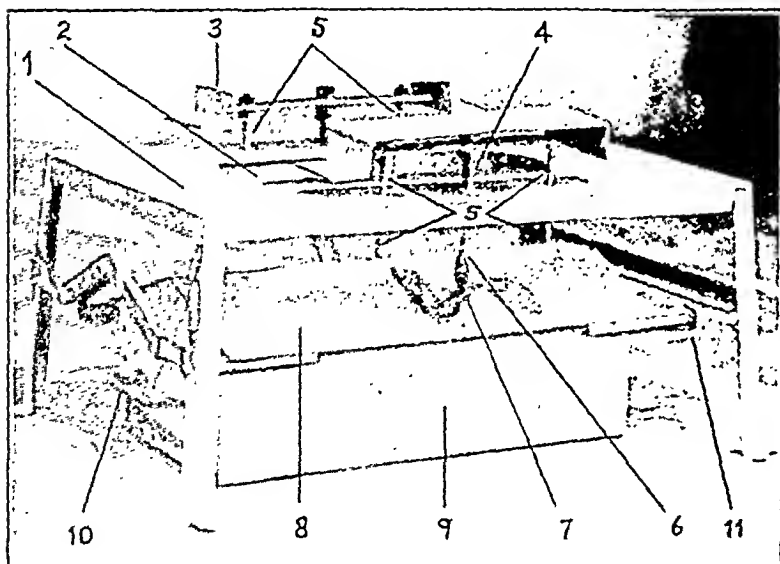


Fig. 3.

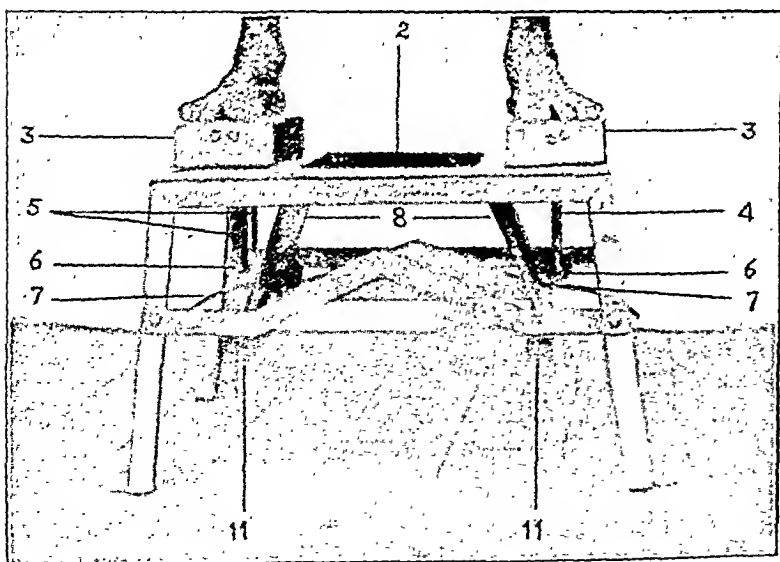


Fig. 4.

## THE INTRADERMAL TEST AS AN INDEX OF VITAMIN-C NUTRITION

### PART II

By SACHCHIDANANDA BANERJEE, M.B., M.Sc.

and

B. C. GUHA, Ph.D., D.Sc.

(From the University College of Science, Calcutta)

IN a previous communication (Banerjee and Guha, 1939) we have attempted to find how far the intradermal test could serve as an index for assessing the vitamin-C status of the body. It was found in controlled experiments with guinea-pigs kept on a scorbutic diet that the time of decolorization increased approximately at the same rate as the body-weight diminished. When a normal diet of ascorbic acid was given

platform (figure 2) and hence cannot be soiled by the user. The lids when fully opened stand at about eighty degrees from the horizontal, and consequently fall down of their own weight and cover the pan as soon as the weight of the feet on the rests is removed. As soon as the user vacates the seat, the foot rests return to their normal position.

It is claimed that :—

1. It is a great improvement on any other latrine of the squatting type.

2. It is sanitary, hygienic, and clean.

3. The excreta in it remains always covered (except when it is actually in use) consequently there is no offensive smell nor has it the unpleasant appearance of an open Indian latrine.

4. As the excreta is covered flies cannot lay their eggs on it.

5. As flies cannot get access to the night-soil, direct infection of food and drink with germs of cholera, typhoid, dysentery, and other fly-borne diseases is not possible.

6. The mechanism is simple in construction, fool-proof and automatic. The hand is not needed for its working and consequently it does not offend caste prejudices.

7. Its cost is low.

8. The only attention that is needed on the part of the sweeper to keep it in working order is the weekly cleaning and oiling of the rods and pulleys under the foot rests. No mechanical device can go on working indefinitely unless some care is paid regularly to its working parts and this seat is no exception to the rule.



to these scorbutic guinea-pigs, the decolorization time gradually diminished and the body-weights rose at fairly equal rates. If the ascorbic acid supplement was withdrawn the weight curve and the decolorization time curve again followed each other approximately. These results received general confirmation also in experiments in which graded doses of ascorbic acid were administered, but the correlation was not quite quantitative.

With human subjects we found that administration of massive doses of ascorbic acid was followed by a peak in the urinary excretion of ascorbic acid; but there was also a reduction of the decolorization time in the skin test. This should not happen if the body were really saturated, as indicated by the peak in the urinary excretion of ascorbic acid. Further work is desirable to explore the relation between the skin test and the saturation test.

As a preliminary, it is necessary to know what the minimum decolorization time would be if a subject is fed with excessive doses of vitamin C, which may presumably correspond to the saturation point. In the present investigation attempts have been made to obtain information on this question by using guinea-pigs under strictly controlled conditions, and normal human subjects.

### Experimental

Three groups of adult male guinea-pigs of weights varying from 400 to 450 gm. were fed on an ordinary diet consisting of green grass and germinated gram supplemented with 2 mg., 4 mg., and 15 mg. of ascorbic acid respectively. The decolorization time was noted. Animals of

the group receiving the daily supplement of 15 mg. ascorbic acid for a period of 14 days were given 40 mg. on the 15th and 16th days and 100 mg. on the 17th, 18th and 19th days in order to find if the decolorization time might be further reduced. The results are given in table I.

It will be observed that, with guinea-pigs receiving the daily supplement of 15 mg. ascorbic acid, the decolorization time is gradually reduced to 1 minute and 30 seconds, which is apparently the minimum time. This is reached within 15 days and the decolorization time cannot be further decreased by the administration of even excessively high doses of vitamin C.

In order to investigate if the feeding of the guinea-pigs with smaller doses of ascorbic acid would prolong the period in which the minimum decolorization time is reached, two groups of guinea-pigs were fed with daily supplements of 2 mg. and 4 mg., respectively. With these two groups the minimum decolorization time was reached after an interval of four weeks. Here also the minimum time was of the order of 1 minute and 20 to 30 seconds. The results are given in tables II and III.

In order to determine if a minimum decolorization time may be obtained with human beings, six healthy adult students of this laboratory were subjected to the intradermal test on one day, and then on the following four days the same test was carried out after the ingestion of 700 mg. of crystalline ascorbic acid on each day. The three hours' urinary test was also studied according to the method of Harris and Abbasy (1937) along with the intradermal test. The results are given in table IV.

TABLE I

*Decolorization time in minutes and seconds in intradermal test on guinea-pigs receiving 15 mg. ascorbic acid supplement daily. The animals were fed 40 mg. ascorbic acid on the 15th and 16th days and 100 mg. on the 17th, 18th and 19th days*

Day	1st		4th		6th		8th		9th		14th		17th		20th	
Number of animal	min.	sec.	min.	sec.	min.	sec.	min.	sec.	min.	sec.	min.	sec.	min.	sec.	min.	sec.
1	3	10	2	45	2	30	1	25	1	45	1	30	1	30	1	25
2	2	10	1	35	1	35	1	30	1	30	1	45	1	20	1	30
3	1	40	2	5	2	0	2	15	1	40	1	25	1	25	1	25
4	2	30	2	15	2	0	2	0	2	0	1	30	1	30	1	30
5	3	40	2	0	2	30	1	30	1	30	1	30	1	30	1	30
6	3	0	2	25	2	0	2	0	2	0	1	40	1	30	1	30
7	2	0	1	30	1	15	1	15	1	25	1	25	1	30	1	30

TABLE II

Decolorization time in minutes and seconds in intradermal test on guinea-pigs receiving 2 mg. ascorbic acid supplement daily

Day	1st	3rd	6th	8th	10th	13th	16th	20th	26th	28th	29th
Number of animal	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.
1	2 30	2 15	2 30	2 15	2 30	2 15	2 30	1 45	1 55	1 30	1 30
2	2 30	2 30	2 10	2 30	2 20	2 40	2 0	1 45	1 30	1 30	1 20
3	2 30	2 15	2 30	2 15	2 30	2 30	2 0	2 30	2 15	1 50	1 20

TABLE III

Decolorization time in minutes and seconds in intradermal test on guinea-pigs receiving 2 mg. ascorbic acid supplement daily

Day	1st	3rd	6th	8th	10th	13th	16th	20th	26th	27th	28th	29th
Number of animal	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.	min. sec.
1	2 30	3 0	2 15	2 10	2 0	2 15	2 10	2 0	2 15	1 30	1 25	1 25
2	4 30	3 0	2 30	3 0	3 0	3 0	2 0	2 0	1 30	1 40	1 25	1 25
3	2 15	2 0	1 30	1 30	1 30	1 30	1 25	1 20	1 30	1 30	1 25	1 25

TABLE IV

Decolorization time in minutes and seconds in intradermal test on normally fed human beings, first day without extra vitamin C and the following four days after the daily administration of 700 mg. ascorbic acid supplement. The corresponding three hours, urinary excretion of true free ascorbic acid is also given

Day	Age	1st		2nd		3rd		4th		5th		6th
Subject		Decolorization time	Urinary ascorbic acid	Decolorization time	Urinary ascorbic acid	Decolorization time	Urinary ascorbic acid	Decolorization time	Urinary ascorbic acid	Decolorization time	Urinary ascorbic acid	Decolorization time
		min. sec.	mg.	min. sec.	mg.	min. sec.	mg.	min. sec.	mg.	min. sec.	mg.	min. sec.
1 (B. G.)	24	2 10	10.4	2 15	3.85	2 10	416	1 45	416	1 30	118	1 30
2 (D. R.)	21	2 30	8.17	2 40	9.11	2 5	470	1 30	248	1 30	156	1 30
3 (J. D.)	21	2 30	13.2	2 30	..	2 20	144	1 35	219	1 30	156	1 30
4 (G. D.)	33	2 0	4.1	2 30	4.5	2 0	11.9	1 35	133	1 30	242	1 30
5 (S. G.)	21	1 5	5.87	1 40	8.41	1 25	416	1 20	391.6	1 25	378	1 25
6 (A. G.)	21	2 0	4.6	2 5	4.55	1 20	200	1 50	350	1 20	146	1 35

From the peak in the urinary excretion of ascorbic acid 24 hours after the ingestion of 700 mg. of ascorbic acid, we find that the individuals were saturated according to the standard of Harris *et al.* (*loc. cit.*). The minimum time of 1 minute 30 seconds, however, was reached on the fifth day of the experiment and not on the third day, which should have taken place if the individuals were really saturated. As the dose of ascorbic acid administered was very high (2.8 gm. per head) and as there was no further reduction of the decolorization time beyond 1 minute 30 seconds, we may

consider that this represented the minimum decolorization time. The value was practically the same as was obtained in experiments with the guinea-pigs.

A statistical analysis on the results obtained, kindly carried out by Mr. K. C. Basak, is appended.

#### Discussion

It has to be observed that the minimum decolorization time in the skin test obtained after heavy dosage with vitamin C was approximately the same (1 minute 20 to 30 seconds) for

both guinea-pigs and human subjects. Further, this minimum decolorization time is reached in human subjects definitely after a peak in the urinary excretion of ascorbic acid has been produced by the administration of massive doses of vitamin C. The question arises as to which method would indicate the saturation of the body with regard to vitamin C. It is clear that even when saturation is indicated by a peak in the urinary saturation test, the skin is still unsaturated as shown by the intradermal test, in which the minimum decolorization time is not yet reached. It is only when this minimum time is reached that the skin may be considered to be saturated with vitamin C. Ascorbic acid being a normal urinary constituent, its increased excretion in urine may not necessarily mean that the individual is saturated. Certain individuals may have a low renal threshold for vitamin C. Further, as the vitamin C in the blood rises, it may be excreted by the kidney, vitamin C having a diuretic effect, and the body-tissues may not have time to become saturated with the vitamin. For this reason it is possible that in many cases no correlation between blood ascorbic acid level and intradermal test-time may be obtained. The skin being a part of the body-tissues its vitamin C, as estimated by the intradermal test *in situ*, might perhaps give a truer picture of the vitamin-C status of the body. Although some workers (Poncher *et al.*, 1938; Goldsmith *et al.*, 1939; Poulsen *et al.*, 1939; Bakhsh *et al.*, 1940) have not observed a correlation between the intradermal test and the blood ascorbic acid level, Suzuki (1939) has observed that the intradermal decolorization time is inversely proportional to the ascorbic-acid content of blood serum, both in normal healthy human subjects and in pathological cases. Beck *et al.* (1939) also consider the intradermal test for determining the vitamin-C supply to be adequate for all practical purposes. As we have, however, pointed out above, absence of correlation, where observed, does not necessarily invalidate the skin test and may readily be explained.

Rotter (1937) has suggested that a decolorization time of the order of 5 minutes indicates that the individual is saturated with vitamin C. From the present investigation this does not seem to be correct. Such individuals may be getting a fair amount of vitamin C but they are not saturated with vitamin C. If the skin test provides a more accurate picture of the vitamin-C status of the body, it is clear that none of the students, on whom tests were carried out in the previous communication (Banerjee and Guha, *loc. cit.*), were saturated. In fact, according to the same standard, vast numbers of people on whom tests have been carried out in other countries, would not seem to be saturated with vitamin C. Thus the whole question of the optimum requirement of vitamin C by human beings appears to require revision.

### Summary

The same minimum decolorization time in the intradermal test is obtained after the administration of massive doses of vitamin C in guinea-pigs and in human beings. This minimum time is 1 minute 20 to 30 seconds. The relation of the skin test to the urinary test is discussed and it is suggested that the minimum decolorization time may perhaps give a truer picture of the vitamin-C status of the body than the urine (saturation) test.

### Acknowledgments

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### STATISTICAL NOTE

By K. C. BASAK

THE two main points to be examined from the observed data of the experiments are:—

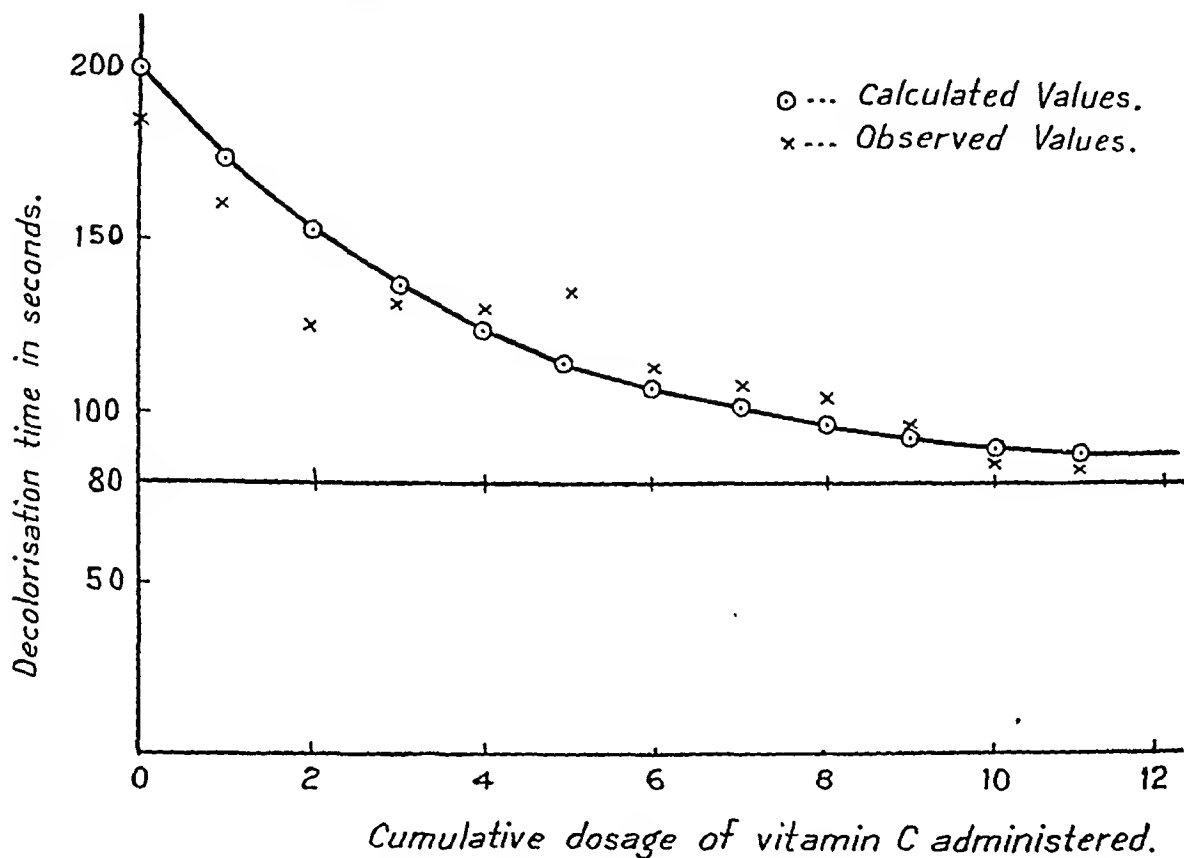
- (1) Whether the decolorization time decreases with increased administration of vitamin C.
- (2) Whether the decolorization time reaches a minimum level indicating the saturation point.

### Experiments on guinea-pigs

The decolorization times on the first day, that is before the ingestion of vitamin C supplement, have been taken as the control figures and their differences from the corresponding observations on successive administrations have been tested for significance. The following table is derived from table I and gives the mean difference, the standard error of difference and the value of *t* at each stage, beginning from the 4th day.

All the values of *t* excepting the first one are significant at the 5 per cent level. The values of the mean difference and standard error appear to be stable from the 14th day, which indicate that on an average the minimum decolorization time was reached on the 14th day. Taking the mean of all the observations from the 14th to the 20th days the minimum time works out as 1 minute 30 seconds.

		Days						
		(1-4)	(1-6)	(1-8)	(1-9)	(1-14)	(1-17)	(1-20)
Mean difference	(in seconds).	30.71	37.14	53.57	45.71	63.71	67.85	67.14
Standard error	..	13.99	10.90	20.23	10.72	15.95	15.42	16.03
t	..	2.19	3.41	2.65	4.26	3.99	4.40	4.19



Similar analyses of tables II and III are rendered difficult by the fact that the number of animals taken for each set of experiments is too small for a reliable estimate of the individual variations of the animals. In table II, however, the mean differences of the observations on the first day with those of the 28th and 29th days are significant. The minimum time, again, is 1 minute and 30 seconds.

In table III the mean difference is not significant at any stage. This is perhaps due to the high variability of the animals before the investigation of vitamin C. An alternative analysis has been attempted to see if the mean decolorization time declined gradually to a level where it remained more or less stable.

An exponential curve  $Y = A + e^{a-bx}$  . . . . (I) is fitted to the mean value of the decolorization time, where Y = decolorization time

and  $x = 0, 1, . . . . .$ , (II) beginning from the first day.

A is tentatively taken as 1 minute 20 seconds. The values of the other two constants, calculated by the method of Least Squares, are

$$\begin{aligned} a &= 4.78 \\ b &= 0.26 \end{aligned}$$

In order to test the goodness of fit, equation (1) is transformed into a straight line equation as follows:—

$$\log_{10} (Y-A) = (a-bx) \times \log_{10} e \dots\dots (2)$$

The observed and calculated values of y are given in the following table:—

Y in seconds			
Serial number	Observed	Calculated	Difference
1	185	200	— 15
2	160	173	— 13
3	125	152	— 27
4	133	135	— 2
5	130	123	7
6	135	113	22
7	112	106	6
8	107	100	7
9	105	95	10
10	93	92	1
11	85	89	— 4
12	85	87	— 2

The regression of the line represented by (2) =  $b \times \log_{10} e = 0.1113$ , and the standard error = 0.0137 therefore  $t = 8.12$  which is highly significant with 10 degrees of freedom.

(Continued at foot of opposite page)

OBSERVATIONS ON THE OUTBREAK OF  
EPIDEMIC CEREBRO-SPINAL MENINGITIS  
IN BURMA WITH A SPECIAL  
NOTE ON ITS BACTERIOLOGY AND  
ON PROGRESS OF THE EPIDEMIC

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CASES of cerebro-spinal meningitis occur annually in Burma in sporadic form and the disease has not been known to take on epidemic proportions for a considerable time past. Therefore when a warning was sounded by the Public Health Commissioner for India in March 1935 forecasting possible epidemics of this disease in Burma 'particularly in a number of urban centres in coming months', the medical and public health authorities had to seek advice from the laboratory workers in regard to specific measures to be adopted in case the epidemic materialized. In offering such advice the main difficulty lay in the lack of knowledge about the type or types of organisms responsible for the past attacks and hence those which would probably give rise to the predicted epidemics. Notwithstanding this handicap group I anti-meningococcus serum raised against Indian strains and the newly prepared

*(Continued from previous page)*

Thus the decolorization time follows a decreasing exponential law approaching a minimum value of 1 minute 20 seconds.

The following diagram shows the closeness of the calculated values to the observed values as the saturation level is approached.

*Experiments on human subjects*

The decolorization times given in table IV have been analysed by the method applied to table I. These figures yield the following table:—

	Days				
	(1-2)	(1-3)	(1-4)	(1-5)	(1-6)
Mean difference in seconds.	6.67	16.67	37.50	42.50	40.00
Standard error.	5.42	6.54	7.90	6.02	6.71
<i>t</i>	1.23	2.55	4.75	7.06	5.96

From the values of *t* it appears that the mean difference is significant at the 1 per cent level from the fourth day. The results of the last two days show a fair degree of stability. It may, therefore, be assumed that on an average the minimum time was reached on the fifth day. The minimum decolorization time may be estimated from the average of all the observations on the fifth and sixth days, which works out as 1 minute 29 seconds.

meningococcus vaccine issued by the Central Research Institute, Kasauli, were considered likely to be useful in an emergency.

At the same time an analysis of the public health records for epidemic diseases in Burma revealed that Rangoon town had annually shown an average of four cases from 1931 to 1934 and that since then there had been a tendency for the figures to go up. Though India had recorded several severe outbreaks in Calcutta, Ahmedabad and Delhi during 1933, 1934 and 1935, here in Burma, in spite of free communication with India, there was no significant variation in incidence of the disease during those years.

From the beginning of 1937, however, definitely increasing numbers of meningitis cases were being admitted into the contagious diseases hospital in Rangoon. This opportunity was utilized to recover cultures of meningococcus from the cerebro-spinal fluid of cases and to study them in details. The work has now been carried on for more than two and a half years consecutively and the results are recorded in the following pages.

At first some difficulty was experienced in getting growths of meningococci in primary cultures on rabbit blood agar medium. But this difficulty disappeared on incubating the cultures under reduced oxygen tension by introduction of carbon dioxide gas, as described by Maitra (1919). Once recovered the cultures were maintained on Dorsett egg medium and when opportunity occurred they were studied morphologically, biochemically and serologically with specific sera obtained from the Standard Laboratory, Oxford. In some cases high titre sera raised at this institute against strains isolated locally were used for cross agglutination tests against type strains obtained from the National Collection of Type Cultures. In this way it has been possible to study 99 strains up to the end of the year 1939. All these strains were recovered from cases occurring within the municipal limits of Rangoon city except one which was recovered from a sample of cerebro-spinal fluid sent from Bhamo in Upper Burma. The organism in the last case survived in the cerebro-spinal fluid the period of transit, which occupied at least four days, without any precautions for regulating the temperature. The case occurred in the month of July when the temperature in Upper Burma is likely to be higher than that in Rangoon.

*Morphological characters of the organisms recovered.*—The growth in primary cultures about 18 hours old on blood agar showed Gram-negative bean-shaped diplococci often exhibiting signs of extensive autolysis. In a stained film many areas could be seen to contain nothing but homogeneous material of cellular debris with occasional diplococci of very swollen appearance. A subculture taken from such a growth and incubated at 37°C. for 12 hours yielded well-formed diplococci in stained films

The signs of lysis were more marked in cultures incubated under a partial carbon dioxide atmosphere.

*Cultural characters.*—As noted before, some difficulty was experienced in obtaining primary cultures at the beginning. But they disappeared subsequently as experience was gained and the technique improved. Papaya-digest agar of pH 7.4 with 10 per cent fresh rabbit blood was used throughout, for cultural work from the cerebro-spinal fluid. Samples of fluid showing very few organisms in film preparations were always incubated for 24 to 72 hours and repeated cultures taken every day. In this way many samples of fluid, which showed no growth at the beginning, subsequently gave positive results. After isolation the cultures were maintained on Dorsett egg medium, as it was found to keep the organisms alive for about three weeks at room temperature, thus obviating the necessity of frequent transfers for maintenance.

*Biochemical reactions.*—These were studied on three sugars, viz, glucose, maltose and saccharose. To sugar solutions in 1 per cent peptone (Witte) water, clear and sterile rabbit serum was added to promote growth of meningococci. After inoculating each strain into a series of the three sugars the cultures were incubated and observed for a week, after which the results were recorded. All the strains studied here fermented glucose and maltose with the formation of acid only. The saccharose remained untouched.

*Reductase reaction.*—We had to modify the method given in Topley and Wilson's book on the principles of bacteriology and immunity in order to get a quick and clear-cut reaction. The broth culture recommended there, in our experience, did not give enough growth to release sufficient enzyme necessary for the test. The organisms were at first grown on blood agar slopes for 18 to 20 hours. The growths thus obtained were scraped off and emulsified in ordinary broth to which one drop of 1 per cent aqueous methylene blue solution was added. The mixture was then incubated at 37°C. for half an hour in a water-bath. Complete decolorization occurred in 10 to 25 minutes, and all the strains, tested, behaved in the same manner.

*Catalase reaction.*—The cultures of meningococci were grown for 24 hours at 37°C. on blood agar slopes. To the tubes set in an inclined position one c.cm. of hydrogen peroxide was poured over the growth. This resulted in an ample production of gas bubbles. All the strains tested reacted similarly.

*Serological reactions.*—So far we have been able to test 99 strains, all collected in Burma including one which was recovered from a sample of cerebro-spinal fluid sent from Bhamo in Upper Burma. The strains were first tested against group agglutinating sera obtained from

Standards Laboratory, Oxford, and the results are summarized below :—

Total number tested	Reacting with group I serum	Reacting with group II serum
99	98	1

The 98 strains belonging to group I were further subdivided into types I and III by testing each of them with a high titre diagnostic serum raised against a known type I strain brought out from the National Collection of Type Cultures. Such strains as agglutinated almost to full titre of the diagnostic serum were classified as the type I strains and those showing only slight or no agglutination with the above serum were classified as type III. Members of type III were further confirmed by their inability to remove agglutinins from type I high titre serum by absorption test. Quite a number of strains reacted almost equally against type I and type III diagnostic sera and they were classified as amphoteric. In this way it became possible to classify 98 strains at our disposal into three main categories as shown below :—

Type I	Type III	Amphoteric (types I and III)
25	61	12

The only strain that reacted against group II serum was subsequently tested against type II serum raised in this laboratory from a known type II culture. As the test culture failed to react it was classified as type IV strain.

It is significant to note here that strains recovered in Indian epidemics of 1934 belonged to group I (Ahuja and Naranjan Singh, 1935) in the same way as the meningococci recovered in Burma, and the association of this group with epidemics in Burma has been constantly maintained for the last three years, during which time the observations recorded in these pages have been carried out. The experience in South Africa where similar observations have been made, however, showed that the type distribution of meningococci recovered from cases of meningitis varied from year to year as would appear from the following table (Ordman, 1939) :—

	1934	1935	1936	1937	1938
Group I ..	24%	9%	60%	57%	64%
Group II ..	76%	91%	40%	43%	36%

*Trend of the epidemic.*—The behaviour of the epidemic was especially studied in Rangoon, a city of about 400,000 population with a substantial number of labouring class people, who



mostly live in small tenement holdings often badly overcrowded. In spite of these conditions multiple cases in the same house were not recorded. In addition to the more or less permanent element there is throughout the year a floating population of immigrant labourers, who pass through the city in search of employment in Burma. Most of these men come from India where epidemic cerebro-spinal meningitis was raging in 1934-35. In spite of this fact no explosive outbreak occurred in the city during those years, as would appear from the statement given below :—

Cases of meningitis in Rangoon

Year		Attacks		Deaths
1934	..	..	4	4
1935	..	..	8	6
1936	..	..	7	5
1937	..	..	27	20
1938	..	..	57	39
1939	..	..	36	16

Though incidence and death increased slowly from 1934 onwards no serious menace occurred like those experienced in Calcutta, Delhi and Ahmedabad between 1934-35. The highest number of seizures recorded in Rangoon city was in 1938 when 57 attacks with 39 deaths occurred, while the corresponding figures in three important cities in India in 1934-35 were as follows (Russell, 1936) :—

		1934		1935	
		Cases	Deaths	Cases	Deaths
Calcutta	..	..	..	814	539
Delhi	..	..	..	508	198
Ahmedabad	..	738	344	..	..

The only instance of a suspected epidemic of fulminating character was reported from some

remote villages in Haka subdivision, Chin Hills District, towards the first quarter, in the Report on the State of Public Health in Burma, for 1937. In four village tracts affected 103 deaths were recorded in course of three and a half months. These villages are inhabited by people of primitive type who reported the deaths many days after they had actually occurred. The public health authorities experienced great difficulty in getting accurate information and the inference of cerebro-spinal meningitis being the cause was drawn mainly from hearsay symptoms. No pathological material could be procured for examination and no record is available as to any of the cases being examined by a qualified doctor.

Summary

1. Epidemics of cerebro-spinal meningitis in Burma were forecast in 1935 but did not materialize till 1937.
2. The epidemic went on smouldering for three successive years in Rangoon and is probably continuing even now. In no instance were multiple cases reported from the same house, though considerable overcrowding and unsatisfactory sanitary conditions were associated with many holdings which returned meningitis cases.
3. Group I meningococci were responsible for this disease in almost all cases which came under observation, and this relationship has been maintained for three successive years 1937-39.
4. A single strain of group II meningococcus was recovered from a solitary case at Bhamo in Upper Burma.

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A Mirror of Hospital Practice

A CASE OF PERITONITIS FOLLOWING ABORTION TREATED WITH SULPHONAMIDE

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I AM prompted to put this case on record because of the patient's surprising recovery from a rapidly spreading peritonitis following on abortion.

The patient was a multipara aged about 35. She had had 11 previous pregnancies all of them going on to full term, but seven children had died under the age

of two years. (Kahn test later showed + + +.) The recent history was that she was five months' pregnant. After three or four days of considerable bleeding, the fœtus and placenta were expelled entire. The next day there was stated to be fever and lower abdominal pain, which increased for two days, when she was brought to the hospital. She had been attended by a village dai with some hospital training. Interference was not admitted.

On admission. 17th March, 1940 (9-30 a.m.).—Temperature 103.4°F. Pulse—104 per minute. Respiration—28 per minute. General condition, poor, dehydrated. The patient complained of severe hypogastric pain. Very slight and not offensive blood-stained vaginal discharge was present. Vaginal examination was not done.

Abdomen: Rigidity and tenderness below umbilicus more marked on right side. The fundus uteri could

not be felt on account of resistance. Upper abdomen not rigid or tender and moving slightly on respiration. The patient had not vomited and was taking fluids by mouth.

Blood count: Hæmoglobin—38 per cent; red blood corpuscles—2,600,000 per c.mm.; colour index—0.7; white blood corpuscles—12,000 per c.mm.; polymorphonuclears—80 per cent.

#### Treatment

17th March, 1940.—Fowler's position. Intravenous soluseptasine 5.0 c.cm. 5 per cent; 1,000 c.cm. saline subcutaneously. Glucose water allowed by mouth 2 to 3 ounces hourly.

Sulphonamide P (B. D. H.), 4 tablets, 11-30 a.m. (Sulphanilamide)

2	"	4-30 p.m.
2	"	6-30 p.m.
2	"	10-30 p.m.
2	"	2-30 p.m.
2	"	6-30 p.m.

Total 7 gm. plus 1/2 gm. intravenously.

Enema given with good result in the afternoon.

Morphia gr. 1/6 at night. Local heat to abdomen.

18th March.—The tenderness had increased in extent to well above the umbilicus and was obviously a spreading peritonitis. There was slight general distension.

All fluid by mouth was stopped and a duodenal tube passed by the nose before there was any vomiting, though the patient complained of nausea, and distension, and inability to pass flatus. Fluid aspirated half hourly was at first bilious and later in the day definitely faeculent in smell and appearance. The patient tolerated the tube well as she stated it relieved the sense of fullness. Subcutaneous saline 1,000 to 1,500 c.cm. was given twice in the day into the submammary and thigh regions. Soluseptasine 5.0 c.cm. was given four hourly by day intramuscularly and four tablets by mouth which were probably not absorbed.

In the afternoon there was almost a classical Hippocratic facies with diffuse tenderness and moderate distension of the whole abdomen and the case was regarded as hopeless. In the evening however the condition appeared to be stationary and it was noted that the fluid aspirated was less in amount and less brown in colour. The temperature remained at 102°F. and the pulse 120 per minute. Morphia was repeated at night.

Blood count: White blood corpuscles 10,600 per c.mm., and the polymorphonuclears were 84 per cent.

19th March.—General condition stationary.

Aspirated fluid less in quantity and gradually clearer and non-faeculent. Three further injections of soluseptasine were given intramuscularly and pituitrin 1/2 c.cm. hourly followed by a flatus tube. On one occasion flatus was passed.

Less distension and tenderness. Tenderness localized again mainly to the right iliac region.

Temperature between 100° to 102°F. Pulse 120 to 130 per minute.

20th March.—Definite improvement. Less distension and tenderness. Duodenal tube removed. Subcutaneous saline continued. A teaspoonful of fluid allowed by mouth, at first two hourly and then hourly. Watery motion passed after pituitrin 1.0 c.cm. Temperature—99° to 101°F. Pulse 100 to 130 per minute. Blood count—white blood corpuscles 6,000 per c.mm. Polymorphonuclears 72 per cent. No sulphanilamide given.

21st March.—Improvement continued. Abdominal signs less. Patient asked for pituitrin again. Injection repeated with passage of flatus and watery motion. Temperature—98° to 99°F. Blood count—white blood corpuscles 4,400 per c.mm. Polymorphonuclears 74 per cent.

22nd March.—Afebrile. Taking moderate amount of fluids by mouth. Blood count: Red blood corpuscles—1,900,000. Hæmoglobin—30 per cent. White blood corpuscles—3,200 per c.mm. Polymorphonuclears—

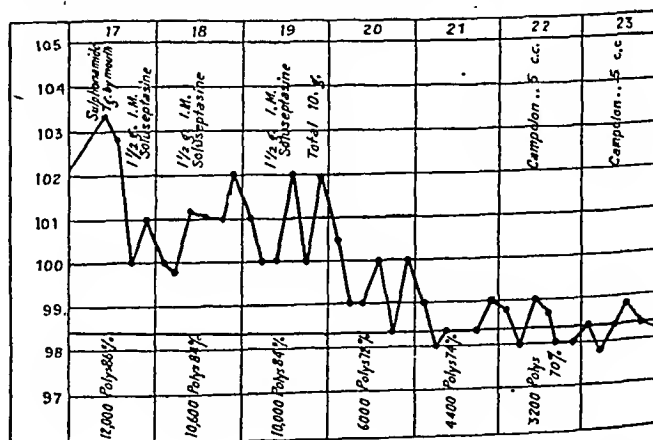
70 per cent. Concern was felt about the fall of leucocyte count and, acting on a verbal report of its value in such cases, Campolon was given daily in 5.0 c.cm. doses for three days and on alternate days in the next week.

23rd March.—Steady improvement. Light diet begun gradually.

27th March.—General condition fair. Fundus could now be felt about half-way between umbilicus and pubis. White blood corpuscles 5,000 per c.mm. Polymorphonuclears 63 per cent. Kahn test + + +. Further progress uneventful.

#### Comment

The conclusions that can be drawn from a single case of this kind are limited. A. J. Cokkinis writing on 'Sulphonamides in Surgical Infections' in the *British Medical Journal* of 29th October, 1938, states: 'My experience with sulphonamide compounds in acute peritonitis suggests that when used correctly chemotherapy may prove of life-saving value, but also that when used indiscriminately it may prove the reverse. The deciding factor again appears to be the immunity response of the patient. Although the cases treated have been comparatively few, they show quite decisively that sulphonamide compounds should not be used as a prophylactic measure against peritonitis in such lesions as perforated ulcer and intestinal strangulation or after operations such as colectomy. They also suggest that it is unsafe to employ chemotherapy in the very early stage of actual peritonitis, that is, while the effusion is still serous and the immunity presumably unawakened. On the other hand, when the more powerful sulphonamide compounds have been administered to cases of fully developed coliform or streptococcal peritonitis with either a profuse purulent effusion or extensive peritoneal oedema the result has usually been a dramatic and lasting improvement. Once started the chemotherapy should be continued for at least ten days but it should never be begun until any removable and unlocalized source of infection has been dealt with by operation'.



The above quotation has been given in full as it acts as a corrective to the impression that might be conveyed by a single successful case. The case reported does, however, confirm that sulphonamide can in certain cases of peritonitis have dramatic effects. The case was the more

surprising, as there was what amounted to faecal vomiting though the fluid was actually drawn off by a duodenal tube as a therapeutic measure.

Other features of interest are—

1. That the chemotherapy was begun late, that is 48 hours after the onset of definite symptoms of infection which is interesting in view of Cokkinis' recommendation that it should be delayed till immunity has been awakened.

2. That the chemotherapy was only continued for three days, a large dose being given by mouth during the first day of treatment, and moderate doses parenterally the next two. The administration was stopped because of the marked clinical improvement associated with a rapid fall in the leucocyte count. In view of the continued clinical improvement and also the progressive further fall of the leucocyte counts, this proved to be justified. A fairly rapid recovery towards the normal occurred when the drug had time to be excreted, but it seems that if the administration had been continued for a week or ten days as is more usual, a grave and probably fatal condition due to the drug would have resulted. This therefore stresses the advisability of very frequent blood, and particularly white cell counts, whenever large or moderate doses of sulphonamide are employed.

3. No information was obtained as to the nature of the infecting organism, but in view of the favourable response to treatment it can be presumed to be one or several of the group known definitely to be inhibited by sulphanilamide, viz, hæmolytic streptococci, certain of the non-hæmolytic streptococci, as *S. faecalis*, *B. coli*, certain pneumococci, gonococci, and possibly certain anærobes as *B. welchii*.

## A CASE OF ANEURYSM OF ASCENDING AORTA

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V. A., male, aged 30, was admitted to the J. J. Hospital with a history of syphilis for which he had had treatment with Bismuthiodol and potassium iodide. He complained of pain in the chest for four months and slight breathlessness on exertion. The pain was in the right side of the chest in front. Occasionally, he said, he also felt it in the inter-scapular region at the back on the right side.

On examination it was found that the veins on the right side of the neck were congested. There was a diffuse swelling (3 inches by 3 inches) with pulsation of the chest wall on the right of the sternum in the 3rd and 4th intercostal spaces extending from the right sternal border almost to the right nipple. This area was dull on percussion. Over it there was an expansile impulse, systolic thrill and bruit. The apex beat was in the 6th intercostal space in the left nipple line. There was a loud ringing aortic second sound. The pulse was collapsing, rapid and regular at both the wrists. The blood pressure was unequal on the two

sides, being 138/68 mm. Hg. in the right arm and 129/76 mm. Hg. in the left arm. The pupils were unequal, the left being larger than the right. The Wassermann and Kahn tests were positive.

Electrocardiographic examination showed left axis deviation. On x-ray examination an aneurysm of the



Fig. 1.—Showing aneurysm of ascending aorta (antero-posterior view).



Fig. 2.—Showing aneurysm of ascending aorta (lateral view).

ascending aorta was seen. Photographs of the antero-posterior and lateral views are given here. They show saccular aneurysmal dilatation of the convex border of the ascending portion of the aortic arch, extending to the right side and in front.

With rest, milk diet and iodides, the patient improved. The pain which was the main symptom was considerably relieved.

The case is of special interest on account of the peculiar shape and position of the aneurysmal sac.

## LINGUATULID INFECTION IN MAN

By D. N. ROY, M.D., D.T.M.

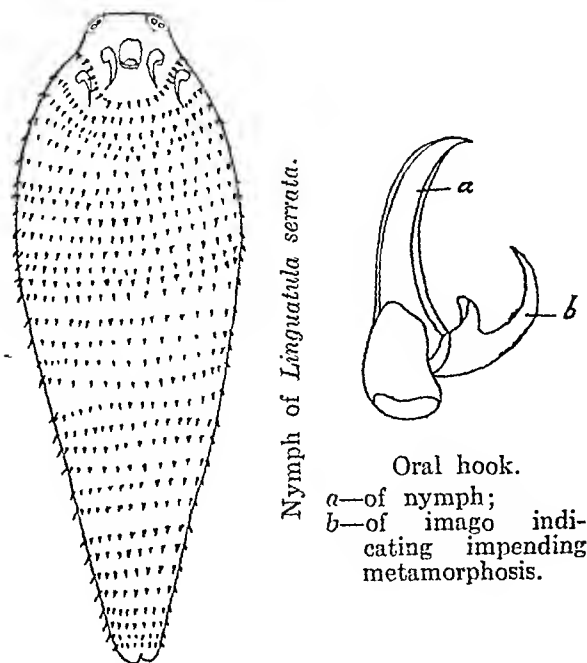
and

S. K. GANGULY, M.B., D.T.M.

Department of Medical Entomology, School of Tropical Medicine, Calcutta

THE only feature of interest in this report is the evacuation by coughing and sneezing of small white 'worms' from the respiratory tract of a female patient whose chief complaints were pain over the region of the frontal sinuses for some time. The specimens were identified as immature stages or nymphs of *Linguatula serrata* Frölich.

The Linguatulids have close affinity with ticks, mites and scorpions, although in their external appearance they resemble segmented worms. The body is vermiform and is markedly annulated. The rings are, however, merely superficial and no trace of any segmentation is present. They therefore are considered as degenerated forms of the Class *Arachnida* and have been included under a distinct Order, *Pentastomida*, which includes among others the family *Linguatulidae*. The life-history of this arthropod includes two hosts, one carnivorous and the other herbivorous. *L. serrata* is found in domestic animals of cosmopolitan distribution and the nymphal form has been reported from cattle, rodents and ungulates.



In *Linguatula serrata*, the eggs are passed in the discharge from the mouth and nostrils; they

also occur in the faeces; when swallowed by the intermediate host the egg-shell is dissolved and the larva is liberated; the larva then bores its way to the liver, spleen, etc., and after a series of moults it encysts, grows and becomes a nymph. When this nymph is swallowed by the final host it makes its way from the gut to the lungs or the nasal cavities where it becomes adult; the nymph, when fully developed, is said to be able to leave the cyst and to migrate to the bronchi or to the intestine of the intermediate host, from which positions it is passed to the exterior. It reaches its final host by being sniffed up by the dog and becomes adult in the nasal cavities (Southwell, 1924).

The nymph has also been frequently recorded from man at autopsy and usually in the liver (Darling and Clark, 1912; Sambon, 1922). In man Landon (Darling and Clark, 1912) reported a case of infection in a blacksmith, producing symptoms pointing to the invasion of the liver by larvae and later an unpleasant sensation of pressure in the left nasal cavity was followed by expulsion of a *Linguatula* with a violent attack of sneezing, thereby relieving all the symptoms of the patient.

The adult is also known as a human parasite but this condition is very rarely met with and appears to be due to embryos wandering into the nose and developing directly.

Among the domestic animals the dog is most frequently attacked and it acts as a definitive host; the adult is lodged in the nasal and ethmoidal sinuses and also in the maxillary antrum.

In view of the fact that there is a history in this case of close association with dogs, it is probable that the infection was acquired from them.

Altogether five 'worms' were collected by the patient in a living state, and they measured on an average 4.8 mm. in length and 1.18 mm. in breadth at its widest part. The rows of spines were 91 in number.

The antrum on illumination did not present any abnormal picture, and the frontal sinuses too looked normal. The cause of pain over the frontal sinuses could not be reasonably explained.

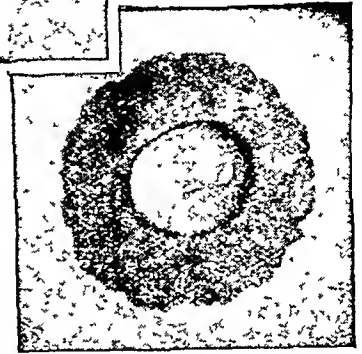
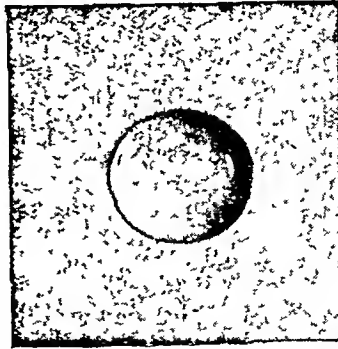
So far we know this is the first record of Linguatulid infection in man in the East.

We are grateful to Dr. S. Roy, M.B., M.Sc., F.R.C.S., D.L.O., Surgeon, Ear, Nose and Throat Department, Medical College, Calcutta, for making the necessary examinations of the nose and the antrum.

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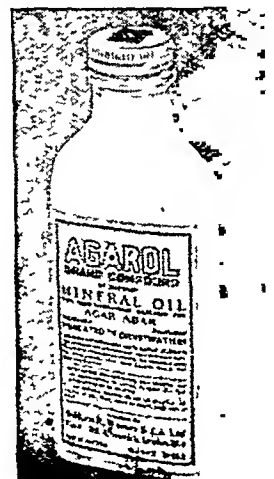
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# Indian Medical Gazette

AUGUST

## AVIATION MEDICINE

A LITTLE over one hundred and fifty years ago man began his first serious attempts to leave the earth and travel through the air, in other words he began the investigation of what is known to-day as aviation. For over one hundred years after his beginning, little progress was made, for during the whole of that time he only had the balloon in which he was unable to direct his journeys but had to rely on the natural air currents, so that the practical value of the air as a means of travel was still negligible. Nevertheless, although the mechanics of air travel were for so long at a standstill, the ill effects on man of a rapid ascent to high altitudes was appreciated in the very early days of aviation, as demonstrated by the ascent of Glaisher and Coxwell in 1862 and the tragic consequences of the historic ascent of Tissandier, Crocé and Sevel in 1875. These unfortunate accidents did not check the progress of man's conquest of the air, but they stimulated the study of the reasons for these ill effects. Paul Bert the French physiologist, who was the pioneer in the study of the effects of alteration of barometric pressure, proved that the principal influence of high altitude was due to the lowered partial pressure of oxygen, and he carried out investigations on questions of respiration and blood gases under decreased atmospheric pressure. 'As a result of Bert's work, which was done directly in connection with these problems of aviation medicine, we cannot help but confer upon him the honour of being the father, or at least the grandfather, of aviation medicine as well as being the first flight surgeon' (Armstrong, 1939).

In the first decade of the present century a beginning was made with mechanically propelled aircraft, and since then the progress in respect of speed, altitude and range of operation of these machines has steadily and rapidly advanced. These mechanical improvements have brought in their train many new complications in the added effects they have on human beings, the study of which is now regarded as a highly specialized branch of medicine. Aviation medicine, however, does not seem to have made much progress during the period prior to the beginning of the last Great War. The Germans alone had been quietly studying the special qualifications required for airmen, and had drawn up minimum standards for military pilots. The English, French and other nations started special medical services for aviators, only towards the close of the war.

During the last Great War it was found that men of physical fitness of the army standard were not necessarily suitable for the air force. In fifty per cent of cases the candidates suffered from neurosis during their training, and accidents were found to be due to the defects in the pilots themselves in 90 per cent of cases. It was thus realized that the selection and medical care of the airmen was a special problem. By the end of 1917 all of the Allies and Germany had medical departments which were integral parts of their air services, and in each were included the leading specialists of the respective countries. The subject of modern aviation medicine has been built up on the work of these pioneers and on that of their successors, all over the world, in the post-war period.

The subject of aviation medicine now includes at least three problems, namely, selection of the pilot, care of the flier, and investigation, prevention and treatment of the diseases that are peculiar to modern aviation, besides research into the newer problems that continue to arise as a result of advancement in design, manoeuvrability and mechanical complications of aircraft, from year to year. The importance of every branch of this subject can hardly be over-emphasized, for the efficiency of a modern air force is almost entirely dependent on it. There is probably no other specialty in medicine at the present time which has so much to offer to the properly qualified physician. No other branch of medicine offers a more fascinating or broader field for research, for no longer is aviation medicine restricted to the selection of candidates for flying training or to the re-examination of qualified pilots, but it includes the study of hygiene, sanitation, epidemiology, aerobiology, physiology, psychology, cardiology, ophthalmology, otology, in so far as these sciences apply to flight. Nor must we think only of the pilot but in addition must consider other members of the crew who are required on large modern aircraft, and of the comfort, health and safety of the travelling public, thousands of whom are in the air every hour of the day and night and whose welfare is a responsibility of aviation medicine.

To India at the present time the subject of aviation medicine is of special interest, in view of the recent decision to build up a large air force. The standards of fitness of fliers, that have been arrived at by experience in other countries, will undoubtedly be of help in the selection of India's aviators, but these standards may not be entirely suitable for this country. The normal physical standards of Indians, regarding height, weight, chest measurements, ocular conditions, power of endurance, etc., are generally different from those of western countries. It is quite probable that the standards for western countries may not prove suitable for this country, and slightly different standards will have to be adopted for the selection of India's pilots. The tropical climate with its

high temperature and humidity, excessive rainfall in some parts and desert conditions in others, will undoubtedly add to the problems of aviation medicine in India. Flight surgeons will have to be trained in India for Indian conditions, and research on the different branches of aviation medicine will have to be carried out locally.

Workers in the aviation industry, who are exposed to noxious fluids and gases and who are liable to serious diseases on this account, will have to be protected from these deleterious substances.

For the solution of the various problems that are likely to arise in the course of development of military aviation in India, the establishment in this country of a school of aviation medicine with aeronautical research laboratories, is a necessity. There is no dearth in India of

specialists in the different branches of medical and physical science that constitute aviation medicine. Every country that has made any progress in aviation, civil or military, has its own school of aviation medicine, where it trains up its flight surgeons. Developments of the present war have brought home to the authorities the necessity of building up an air force for India. If it is to be of any use, the air force will have to aim at superiority over other eastern countries and a huge personnel will have to be trained and equipped. This makes the establishment of a school of aviation medicine in India all the more important and urgent.

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## Special Articles

### HÆMATOLOGICAL TECHNIQUE

#### PART V

By L. EVERARD NAPIER, F.R.C.P. (Lond.)

and

C. R. DAS GUPTA, M.B. (Cal.), D.T.M.

(From the Calcutta School of Tropical Medicine)

#### *Hyperbilirubinæmia and van den Bergh's test*

BILIRUBIN is normally present in small quantities in blood plasma and blood serum, and their yellow colour is in part due to this substance.

Ehrlich observed that when sulphanilic acid and sodium nitrite were added to a solution of bilirubin, a bluish-violet substance, azo-bilirubin, was formed. The reaction is specific and will show bilirubin in a dilution of 1 in 1,500,000.

Van den Bergh made use of these observations, not only to test for the presence of an excess of bilirubin, but to draw certain conclusions from the nature of the result. His original claims are now questioned, but his general conclusions hold good and form the basis of the test which we are describing.

Bilirubin is a by-product of hæmolysis. It is normally present in the blood in a dilution of about 1 in 400,000 or 0.25 mg. in 100 c.cm. of blood. It is excreted *via* the bile ducts after passage through the parenchyma cells of the liver; during its passage through the liver cells the blood bilirubin loses its protein molecule. If the passage of the bile is obstructed (obstructive jaundice), the bilirubin from the bile is reabsorbed into the blood stream; this bilirubin, stripped of its protein molecule, reacts readily with the diazo reagent and gives what is known as a direct reaction.

In conditions of excessive hæmolysis and/or liver dysfunction, the amount of bilirubin present in the blood naturally increases; the

diazo reagent does not react with this blood bilirubin immediately but only after it has been in contact with it for some time (this is sometimes known as a *delayed direct reaction*, but this reaction is not usually taken into consideration as it has no special significance beyond that covered by the indirect reaction which is clearer and susceptible to quantitative appraisal *v. i.*). However, if the serum has been treated first with alcohol and the protein precipitated, an immediate reaction occurs; this is known as the *indirect reaction*.

A third type of reaction is that in which there is an immediate faint colour which steadily increases, indicating that both forms of bilirubin are present; this is known as the *biphasic reaction*.

The technical details of the test have been modified many times and it is done in a number of ways in different laboratories. Godfried (1935) recommends the method described by Thannhauser and Andersen (1921) as the most suitable for clinical purposes; this is the method that we follow in our laboratory.

#### *Apparatus required*

Graduated pipettes, 1 c.cm., 2 c.cm., 5 c.cm., and 25 c.cm.

Small test-tubes, 4 inches by  $\frac{1}{2}$  inch.

Centrifuge tubes.

Small glass beakers or flasks.

Capillary pipettes with rubber teats.

Centrifuge machine.

Sealed cobalt sulphate standard tubes.

\* Lovibond comparator with the coloured discs for bilirubin.

#### *Reagent*

Alcohol—absolute and 90 per cent.

Saturated solution of ammonium sulphate; this is prepared by dissolving an excess of ammonium sulphate

\* The comparator may be obtained from Tintometer Ltd., Milford, Salisbury (U. S. A.), or from the British Drug Houses Ltd., London.

in hot water (so that some undissolved salt is left at the bottom).

Normal saline.

*Diazo reagent*

- (A) Sulphanilic acid—1 gramme.  
Concentrated hydrochloric acid—15 c.cm.  
Distilled water 1,000 c.cm.
- (B) Sodium nitrite—0.5 gm.  
Distilled water 100 c.cm.

Stock solutions of (A) and (B) are made. They keep well for a long time.

The test can be done either with the serum or plasma. When the cell volume is also being estimated, the supernatant plasma in the cell-volume tubes, after the packing of the red cells, is quite sufficient for the test. When the test is done by itself, three cubic centimetres of blood is drawn in a dry test-tube or an oxalated tube.

The blood is collected in the usual way, and even the slightest hæmolysis must be avoided (part I). Preferably, the blood should be collected in the fasting state as it is claimed that food intake, especially a big meal of carbohydrate and fat, affects the level of serum bilirubin. The specimen must always be examined within two hours, as otherwise paradoxical results may be obtained.

*Technique.*—Prepare the diazo reagent by mixing 10 c.cm. of A and 0.3 c.cm. of B in a small flask or beaker.

This mixture must be prepared just before use and must never be used later than one hour after it is made.

Pipette off the clear supernatant plasma from the cell-volume tubes.

*Direct reaction.*—Take exactly 1 c.cm. of plasma in a centrifuge tube.

Add exactly 0.5 c.cm. of diazo reagent, and mix well.

One of the following things may happen :—

(i) Direct reaction—The mixture becomes bluish-violet within 30 seconds.

(ii) Bi-phasic reaction—The mixture becomes slightly reddish at once and the colour gradually increases in intensity and becomes bluish-violet.

(iii) Negative result—No change of colour occurs within 10 minutes.

*Indirect reaction.*—If no change occurs (iii), add to the mixture of plasma and diazo reagent 2.5 c.cm. of alcohol (absolute or 96 per cent), and 1.0 c.cm. of saturated solution of ammonium sulphate.

Mix well by inverting the tube, and allow it to stand for about two minutes, and centrifuge for 5 to 10 minutes.

A positive indirect reaction is indicated by the supernatant fluid becoming coloured a distinct bluish-violet, the intensity depending on the amount of bilirubin present. As bilirubin is present in normal blood, a faint violet colour nearly always appears and obviously has no pathological significance.

*Quantitative indirect reaction.*—It will be clear that some form of quantitative estimation is essential. Many elaborate methods which require special apparatus have been devised, but a fairly accurate estimation of the bilirubin content can be obtained by carrying out the test in the way described above and comparing the supernatant fluid with a prepared standard or with a permanent colour standard.

(i) Comparing the supernatant coloured fluid with the cobalt sulphate standard (2.161 per cent) has given the most satisfactory colour matching in our hands.

*Preparation of the cobalt standard solution.*—Dissolve 2.161 grammes of anhydrous cobaltous sulphate in distilled water. The colour of this solution corresponds to that of 1 in 200,000 bilirubin or 0.5 mg. of bilirubin per 100 c.cm. Solutions equivalent to 0.4, 0.3, 0.2, 0.1 and 0.05 mg. per 100 c.cm. are made by diluting the original solution.

About 2 c.cm. of each of these solutions is put into tubes made of hard glass. The tubes are then sealed, numbered, and kept in the dark, and are brought out only when required. Properly stored, the solutions retain their colour for a fairly long time. In our laboratory, we did not find any difference in colour in solutions which were in daily use for over six months, when these were compared with freshly-prepared solutions.

*Technique for the use of cobalt standard solution.*—Take about 2 c.cm. of the coloured supernatant fluid in a tube having identically the same bore as the standard tubes, and compare its colour in a comparator with the cobalt standard tubes. The figure on the tube giving the correct matching with the supernatant fluid multiplied by four gives the bilirubin value of the undiluted serum, for the dilution of the serum in the supernatant fluid containing azo-bilirubin is 1 in 4 and not 1 in 5, because the saturated ammonium sulphate remains as a separate layer and does not contain azo-bilirubin.

If the supernatant fluid is of a deeper colour than the cobalt standard tube marked 0.5, dilute the supernatant solution with normal saline (dilution with 67 per cent alcohol which is recommended makes the solution hazy and difficult to match) until it matches one of the cobalt standard tubes. Note the dilution required to match and calculate the amount of bilirubin in the specimen.

*Example.*—One cubic centimetre of supernatant fluid was taken to which was added 1 cubic centimetre of normal saline to match the tube marked 0.4.

First dilution of serum in the supernatant fluid is 1 in 4.

Second dilution to match the colour is 1 in 2.

Therefore, total dilution is  $\frac{1}{4} \times \frac{1}{2} = \frac{1}{8}$ .

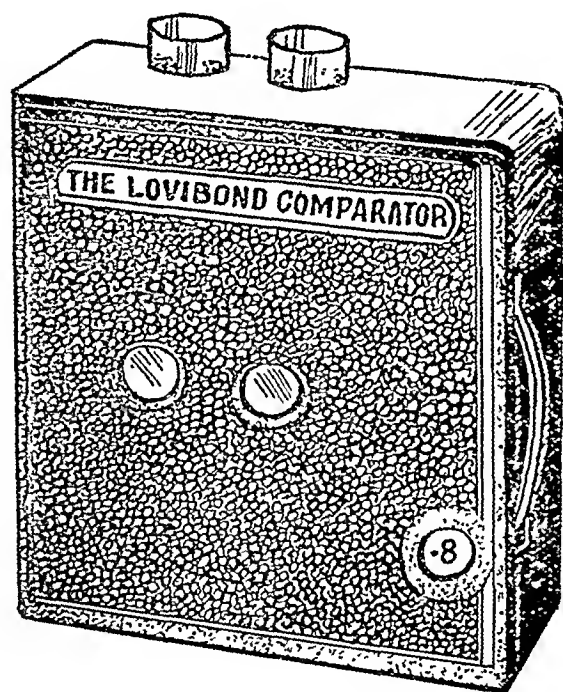
Then the original plasma contained  $0.4 \times 8 = 3.2$  mgm. of bilirubin per 100 c.cm.

(ii) *Lovibond comparator*.—Quantitative estimation of the indirect van den Bergh reaction can be simplified by the use of a bilirubin disc in the Lovibond comparator. The disc contains coloured glass standards marked 0.2, 0.4, 0.6, 0.8, 1.0, 1.25, 1.50, 1.75 and 2.0 mg. which are calibrated in such a way that, when the test is done in the way described above, the matching with any of the discs gives directly the result for the undiluted serum (figure).

*Technique for the use of the comparator*.—Fit in the disc marked 'bilirubin' in the Lovibond comparator. Transfer the coloured supernatant fluid to the right hand tube of the comparator. A tube of distilled water should be put behind the hole showing the coloured glass. Hold the comparator against a source of light (daylight is much better than any artificial light). Rotate the disc till a correct colour

### Normal bilirubin

Author	BILIRUBIN IN MILLI-GRAMMES PER 100 C.C.M. OF PLASMA OR SERUM		
	Range	Mean	S.D.
Van den Bergh (Vaughan and Haslewood, 1938).	0.08-0.24	..	..
Greene <i>et al.</i> (1925)	0.3-2.0	..	..
Perkin (1927)	0.05-0.35	..	..
Barron (1931)	0.1-0.24	..	..
Elton (Vaughan and Haslewood, 1938).	0.0-0.25	..	..
Vaughan and Haslewood (1938).	0.2-1.7	0.54	± 0.25
Mills and Mawson (1938)	0.1-1.0	0.31	± 0.16
Napier and Das Gupta (1940) (in preparation).	0.0-1.0	0.02	± 0.23



Lovibond comparator with the bilirubin disc and tubes in position.

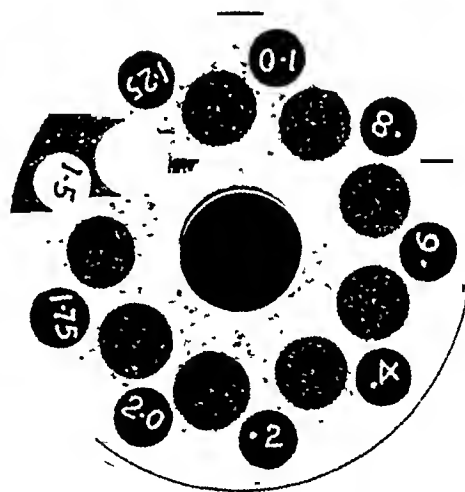


Fig.

Bilirubin disc for the Lovibond comparator.

match is obtained, the number in the disc indicates the bilirubin value in mgm. per 100 c.cm. of undiluted serum or plasma.

When the colour of the supernatant fluid appears to be between two consecutive coloured discs and does not exactly match either of them an intermediate value is recorded.

If the bilirubin value exceeds 2 mgm. per 100 c.cm., dilute the supernatant fluid with normal saline until a correct match is obtained with one of the coloured glasses. Calculate the bilirubin value by multiplying the number on the disc by the dilution factor.

### Icterus index

Like the van den Bergh reaction, the icterus index is a measure of the bilirubin content of the blood. Though the test is simple to carry out, it does not give all the information which is obtained by the van den Bergh test.

*Principle of the test*.—The colour of the serum or plasma is compared with a standard solution of 1 in 10,000 potassium bichromate, which is taken as the unit.

### Apparatus required

Test-tubes in a rack.  
Capillary pipettes with rubber teats.

Potassium bichromate solution 1 in 10,000.  
(To be stored in the dark).

Colorimeter of the Dubosq or Klett type.

*Technique.*—Pipette off the supernatant plasma from the cell-volume tube after complete packing of the cells.

Dilute the plasma with an equal part, or with twice the amount of normal saline (more in cases of jaundice); dilution diminishes the cloudiness of the plasma and gives a better matching.

*Matching in the colorimeter.*—The following adjustments of the scales and of the illumination must always be made each time before the use of a colorimeter.

(i) Adjustment of the scales. Gently raise the cups until the bottoms are in contact with the plungers. The readings should be exactly at 0 on both sides. If they are not, they must be brought to 0 by adjustment.

(ii) Adjustment for uniform illumination. Half fill both the cups with the standard 1:10,000 potassium bichromate solution. Gently raise the cups until the bottoms touch the plungers—this will drive out any air bubbles that may be in the fluid.

Now slowly bring down the cups and set them at an equal depth, say 15 millimetres. Adjust the reflector in such a way that the same amount of light is reflected up through each cup.

Slight adjustment of the eyepiece may be necessary, if both halves of the field do not match exactly.

*Taking a reading.*—Keep the cup on the left side at a depth of 15 millimetres.

Take out the cup from the right side, throw out the potassium bichromate solution, wash the cup thoroughly in water, dry it well with soft linen. Put the diluted plasma into the cup and replace it on the right side of the colorimeter. Gently raise the cup until its bottom touches the plunger. Now move this cup containing the plasma up and down until a perfect match is obtained; take a reading. Move the cup up or down and again adjust it to match; take another reading.

Take the mean of three independent readings.

### Calculation

Icterus index =

$$\frac{\text{Reading of standard bichromate sol.}}{\text{Reading of diluted plasma solution}} \times \text{dilution factor.}$$

*Example.*—One part of plasma is diluted with two parts of normal saline.

The cup containing the standard solution is at 15 mm.

The cup containing the unknown plasma matches the standard at 5 mm.

Icterus index— $\frac{1}{2} \times 3 = 9$ .

B. *Matching in tubes.*—In the absence of a colorimeter, results sufficiently satisfactory for clinical purposes may be obtained by matching the plasma or serum diluted with normal saline

against the standard 1:10,000 potassium bichromate solution.

Take two test-tubes of equal height and calibre. Into one put about 5–10 c.cm. of standard potassium bichromate solution. Into the other put 1 c.cm. of plasma and add measured amounts of normal saline from a graduated pipette until the colour matches the standard.

*Calculation.*—The dilution of the plasma required to match the standard potassium bichromate solution gives the icterus index.

*Example.*—To 1 c.cm. of plasma was added 7 c.cm. of normal saline to match the standard. Dilution of the plasma is 1 in 8. Therefore, icterus index = 8.

Normal icterus index, 4 to 7.

*Discussion.*—The significance of the van den Bergh test in hæmatological investigation is that it gives a *broad* indication as to whether the anæmia is due to excessive blood destruction or deficient blood formation.

In the true hæmolytic anæmias the test always gives a high reading, 2.0 milligrammes or more, in iron-deficiency anæmias it is within normal limits, and in aplastic anæmias it may be completely 'negative' (in the normal individual there is usually a faint violet coloration of the serum).

In pernicious anæmia a reading well above the normal range is usual, for, though it is not a true hæmolytic anæmia, the deficiency of 'hæmopoietin' leads to the formation of abnormal cells which are very susceptible to destruction by the normal hæmolytic tissues.

In tropical macrocytic anæmias, in a large number of cases, especially in those with enlarged spleens, the test is much above the normal range and in a small number of cases the test is well within the normal range.

It is not, however, an absolute indication, either of excessive blood destruction or of deficient blood formation as, for example, in an acute malarial attack, when there may be enough red cells destroyed to lower the red cell count a million or more cells per c.mm., the van den Bergh often remains within normal limits, for the liver cells are able to excrete this temporary excess of bilirubin in the blood, but if the red cell destruction is continued the bilirubinæmia will inevitably rise above the normal range and a 'positive' van den Bergh reaction will result.

On the other hand, in liver dysfunction, not necessarily accompanied by anæmia, a positive van den Bergh may be found, for the liver cells are unable to utilize the products of normal hæmolysis.

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(Continued at foot of next page)



## 'DOPING' IN ATHLETIC CONTESTS

By E. S. PHIPSON, C.I.E., D.S.O., V.H.S., M.D., F.R.C.P.  
COLONEL, I.M.S.

ONE of the most remarkable developments in the field of athletics in recent years has been the growth and popularity of the international athletic contests on a grandiose scale which are known as the Olympic games.

For many years past these contests have been staged and produced on an ever-increasing scale of lavishness, and though the healthy spirit of emulation engendered by the aggregation of the world's finest athletes is sometimes clouded by jealousy, recrimination and even international 'incidents', there can be few who would not agree that, in theory at least, such contests are the expression of a worthy and even a noble ideal, even if, in practice, they do not always attain to the lofty standard which, we presume, characterized the Olympic contests in the golden days of ancient Greece.

These contests, however, have more than one disadvantage; not the least of these is the almost morbid craze for record-breaking to which they have given rise, and which has brought in its train an eager search for means, some rational and harmless, others dubious or indefensible, to raise the level of athletic performance to a standard otherwise unattainable. These means are collectively known as 'doping'.

The subject of 'doping' has recently been examined in the Laboratory of Theoretical Studies on Physical Training in the University of Copenhagen, and the present communication is based on Dr. Ove Bøje's examination (1939) of the very considerable literature, mostly German, on this little-known subject, published by the Health Organization of the League of Nations.

Resort to means to enhance the powers of endurance is no new device. Everyone has heard of the use of opium for this purpose in India, and of coca-leaves by the Indians of South America. In bygone times the Samoyeds and the Berserkers are said to have consumed a muscarin-containing mushroom to rouse themselves to the required degree of combativeness before going into battle. The word 'doping' is now used in a general sense to denote any method of temporarily improving athletic performance and includes not only the use of powerful drugs but also dietetic preparations, non-toxic salts, oxygen and ultra-violet radiation, and it might even be said to include massage and the purely psychological means

of encouragement shouted to competitors during the actual course of a contest.

It is evident that there is a wide difference between 'doping' a competitor with, for example, a feed of glucose and with highly active and toxic drugs such as cocaine or cardiazol. The extent to which it is permissible on ethical grounds, that is from the standpoint of 'sportsmanship', to use such means to improve the athletic performance of a team or of an individual is a matter which must be left to the leaders of athletic associations to decide, or ultimately, perhaps, to public opinion, though the lengths to which certain trainers and athletes will go in pursuit of a coveted record can hardly be in the ancient Greek tradition. From the purely medical standpoint, however, the strange aspect of 'doping' is, on the one hand, the variety of drugs and other means employed, and, on the other, the resilience of the human organism to maltreatment of this nature, for in many cases it is little less, and these present a curious sidelight on pharmacology. The writer believes it will be of interest to summarize the various means employed and the effects they are believed, or have been found, to produce on athletic performance.

1. *Food-preparations and non-toxic salts.*—Since prolonged muscular work leads to a fall in blood-sugar, and if pushed to extremes, to an acute hypo-glycæmia, the administration, during the course of an experiment, of *carbohydrates*, in the form of glucose, or even cane-sugar, will defer exhaustion-point by as much as a full hour in some cases, but there is nothing to show that the ingestion of glucose in considerable quantities before the experiment or contest will have the same effect. *Lecithin*, in the form of egg-yolk, or in the form extracted from soya-beans, has been largely used but on experimental evidence its value is doubtful. *Vitamin B<sub>1</sub>*, in the form of yeast, since it plays a part in carbohydrate metabolism, and if taken with glucose assists in the accumulation of glycogen reserves in the liver, might be expected to favour prolonged muscular effort, but there is no proof that, although a sufficiency of B<sub>1</sub> is, of course, necessary for health, an excess of it will raise functional capacity.

The preliminary ingestion of *phosphates* has apparently been proved in many experiments to increase substantially the output of work, in some cases by as much as 20 per cent, particularly if it is taken in the form of the widely-advertised German preparation 'Reeresal' in which the intrinsic effects are no doubt increased by the psychological effects of intensive advertising. The conclusion appears to be that phosphates, taken in excess of dietetic requirements, actually increase muscular output, and are harmless unless taken in massive doses.

Heavy physical effort in great heat entails a loss of salts, particularly of *sodium chloride*, and replacement is known to be essential in conditions such as heat-cramp, but in athletics

(Continued from previous page)

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signs of salt deficiency are likely to become apparent only in long contests, carried out in warm weather. Ingestion of salt would correct this, but its value would have to be balanced against its thirst-producing tendency. The salt-content of a highly trained athlete's diet is usually cut down on this account. *Alkalis* have frequently been used and the experimental evidence on the whole indicates that an artificially-induced alkalosis, in some cases at least, increases physical efficiency and output, presumably by neutralizing excess of lactic acid produced by muscular action.

*Ammonium chloride*, though not hitherto used in athletic contests, is of established value in resisting the effects of high altitudes in aviation and in mountaineering, and in moderate doses appears to be quite harmless. Haldane's explanation of the beneficial effect of ammonium chloride is interesting: the low oxygen pressure resulting from high altitudes causes increased respiration and this causes the amount of carbonic acid expelled by the lungs to rise; the consequent alkalosis then inhibits any further increase of pulmonary ventilation. The administration of ammonium chloride retards the development of this alkalosis; the degree of ventilation can therefore rise further and the alveolar oxygen pressure can increase.

2. *Administration of oxygen*.—A considerable amount of experimental work has been carried out on the value or otherwise of oxygen in athletic contests. At the last Olympic games the Japanese swimmers were said to have been 'pumped full of oxygen' in their dressing-rooms immediately before the races started, and this led to discussions in the press on the value and on the propriety of 'oxygen-priming' as it is called. Different investigators have recorded widely different conclusions on this subject, and in general it may be stated that it is highly questionable whether 'oxygen-priming', under the conditions which must obtain in actual practice, is of any value in sports events, except, possibly, under-water swimming. All observers seem to be agreed that it is at least harmless.

3. *Artificial sunlight*.—Experimental investigation shows that exposure to ultra-violet radiation endows the organism with an increased capacity for work, and if administered in suitable doses and kept within moderate limits it should not present any dangers. Signs of marked fatigue may follow the first sittings; only after some time will an improved zest for exertion and an increased sense of well-being make their appearance.

4. *Administration of pharmaceutical substances*.—This group comprises many drugs which are very poisonous, the use of which represents at present the extreme limits of 'doping'.

*Alcohol* has a very limited range of utility as its toxic effects overshadow the part it plays as a source of energy, and it has been conclusively

shown that every type of physical work associated with mental effort or requiring delicate muscular co-ordination, is unfavourably affected by alcohol. The best that can be said of alcohol is that, as regards purely muscular effort, it may cause a transitory increase in output, followed later by an inevitable lowering of efficiency, and these characteristics of alcohol are generally recognized in the world of athletics. *Ammonia* in the form of smelling-salts is a well-known and harmless stimulant of the central nervous system acting through the nasal mucous membrane; it is widely used by boxers between the rounds of a contest. *Cocaine* is one of the oldest and most dangerous forms of 'dope'. Like opium in India, cocaine is used in South America by miners and others performing heavy physical labour under particularly arduous conditions. It has also, it appears, been largely used by athletes in contests demanding extreme powers of endurance, such as six-day cycle races. Its effect on metabolism is uncertain and probably unimportant; it is mainly effective by removing the sensations of fatigue and hunger, so that heavy work can be performed for very long periods. The dangers to the individual of the abolition of nature's safety-valve, fatigue, to say nothing of the great risk of addiction, are so manifest that the use of cocaine in connection with athletics ought to be prohibited. No Olympic laurels could be weighed in the balance against the tragedy of even one case of cocaine addiction.

*Caffeine* and other purin-derivatives are, of course, commonly used in the form of tea, coffee, cola and chocolate as well as in the pure state as stimulants in connection with physical and mental effort, and there is ample experimental evidence that drugs of the caffeine group actually increase the capacity for sustained effort and defer the exhaustion-point. It is questionable, however, whether drugs of this group can be administered in their pure state without risk to health, though there is no reason to avoid them in the form of tea, coffee and chocolate. *Benzedrine* is capable, even more than caffeine, of eliminating the sensation of fatigue, particularly in tests involving intellectual work, but its effects on muscular work have not so far been fully studied, and there is no evidence that performance is improved. The secondary effects which so often accompany its administration, such as tachycardia, vertigo, restlessness and insomnia, are of such a character that, apart from the risk of eliminating fatigue-sensation, the drug is not suitable for use in connection with athletics.

Since the circulatory system often sets a limit to athletic performance efforts have been made to increase the range of circulatory efficiency by the use of drugs acting on the circulation. *Digitalis* has been tried but, as might be expected, appears to have no action on a healthy heart subjected to abnormal exertion, and its

use, perhaps fortunately, seems to have been abandoned, as it cannot be considered an innocuous drug. *Nitroglycerine* is sometimes used in sprint cycle races and is said to relieve shortness of breath after violent efforts of short duration, but its secondary effects, such as vertigo, vomiting, hypotonia and even circulatory collapse, are so formidable that few athletes are likely to take it more than once, except in minimal doses. *Coramine* and *Cardiazol* have been extensively used by athletes in recent years for their stimulating influence on the circulation and central nervous system, and for the subjective feeling of freshness which they induce in the tired organism, and there is some evidence that there is an actual and objective increase in the capacity for prolonged effort. The use of drugs of this character cannot be considered harmless; they are known to possess convulsive properties apart from the risks of the attenuation of the normal regulative action of fatigue, which is the main purpose for which they are used.

*Hormone* treatment for healthy athletes has been employed. The British Press not long ago announced that the remarkable performances of the Wolverhampton Wanderers football team were due to 'gland extract' treatment provided by their enterprising manager, and the Portsmouth team decided to follow their example. The nature of the extract used was not stated, but it was understood to be a testicular extract, and if so, their improved performance might well have been due to the purely psychological effect of such treatment. The administration of oestrus-producing substances to women athletes is on a rather different footing. It is used to alter the time of onset of menstruation if this should coincide with the date of the contest, and it appears to be effective. It is doubtful, however, whether even that degree of interference with natural processes can be undertaken without risk to health.

To sum up, there are a considerable number of substances which athletes actually use or are urged on them by their trainers; in some cases their use does not endanger health, in many other cases they are known or believed to be injurious. The principle should evidently be to avoid the use of any stimulants whose action is directly associated with risks of toxic effects and indirectly with the danger of 'whipping up' the organism to extreme exertion. The least objectionable group would seem to be the nutrient preparations, non-toxic salts and oxygen.

The ethical considerations of 'sportsmanship' involved in the use of these or other means of artificially raising the level of athletic performance can be left to public opinion and it is to be hoped that if 'doping' is carried to further extremes public opinion can be trusted to rebel.

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## MEDICAL NOTES FROM THE DIARIES OF THE THREE SURGEONS OF PATNA—1763

By D. V. S. REDDY  
*Vizagapatam*

THE diaries of Anderson, Campbell and Fullerton commence from the last week of June 1763, when matters were rapidly coming to a crisis between the English and the Nabob of Bengal. These journals faithfully record the eventful days of the massacre of Patna . . . and the other associated disasters, till the arrival of the victorious English Regiment under the command of Major Adams.

The diaries start from 23rd June, 1763, the anniversary of the battle of Plassey. Certain feverish activities in the English camp and the anxious look of the important actors in the drama, betrayed that the English colony at Patna were apprehending some immediate danger.

Next day Patna was attacked by the English. Fullerton wrote on this day as follows:—'About 10 o'clock at night on the 24th Mr. Ellis sent for me from the *Hospital* and ordered that the sick might be embarked in boats and carried over to the sand opposite to the city and from thence tracked up and crossed over to the factory'. Fullerton was to embark at 2 a.m. just the hour fixed for attacking the city. This plan was accordingly executed. The sick consisting of 23 Europeans reached the factory at 9 a.m. the same day (25th). Campbell also made the following entry:—'Numbers of *wounded men* were coming out of the city which employed Fullerton and Anderson and myself for the day'. Fullerton graphically describes the wretched condition of the English factory after the failure of the attempt to gain control of the City of Patna. Some Europeans and 100 sepoys were wounded. 'The confusion of such a number of troops (nearly 2,000) with the sick and wounded in so small a place as the factory, must be easily imagined'.

On the 26th, they got as many boats as they could and embarked at night with the sick Europeans and the factory treasure of one lakh. Dr. Campbell who was marching with the army also writes under 27th June:—'Most of the boats proceeded up the river with the *wounded Europeans* (looked after by) Drs. Fullerton and Anderson'. Anderson's diary also has a note dated 27th, 'Accordingly the sick, the treasure and the howitz with part of the ammunition, were to go by water, for want of coolies while the army marched by land. On account of the sick, I went by water'. Dr. Anderson was much disappointed that evening. 'For, the boat with my clothes *instruments, medicines* and servants did not arrive so that I imagine this must have been stopped'.

On 1st July, Captain Carstairs was injured by a shot (*Jinjal* ball). He was one of the

English heroes of the siege of Calcutta and the battle of Plassey. Anderson thus writes on this topic : 'An unlucky shot hit Captain Carstairs as he was sitting down. It entered the inside of his thigh and passed out at his loins (groins). From the nature of it, it must be mortal'. Campbell also notes under date 1st July :—'About 11, we had the disagreeable news of poor Carstairs being *mortally wounded*. He was soon after brought over and *upon dressing him I found the wound to be mortal*. He was brought aboard Captain Wilson's *budgero* and *begged of me that I would not leave him*'.

Later in the day, when the enemy began a severe fire and vigorous onslaught, the boat which carried Captain Carstairs, Dr. Campbell and Anderson pushed off to a distance and tried to run up to Patna. The boat ran aground on the way; they were wavering to go ashore or not. 'But could not think of leaving Carstairs who though mortally wounded was perfectly sensible. It must have added to his uneasiness to have his friends leave him helpless in such distress'. Next morning, the boat was hailed by a party of the enemy and after some consultation, the boat proceeded further down the river and arrived at Hadgipore, where they were kindly received by *Phousudar's son*. Campbell wrote the following note on the same day : 'Carstairs continues to grow worse every hour'. Fullerton was sent to Patna where he was received kindly by the Nabob. It was from Patna, where he was kept a prisoner in the *killa*, that Fullerton wrote a note to the English party at Hadgipore to come down to Patna, lest the country people might treat them harshly. They came and among them were Anderson, Surgeon and Peter Campbell. Anderson and Campbell, who were with Carstairs till his death on 3rd July, add further details. Anderson wrote :—'Poor Carstairs died *on shore at a small house* that had been provided for him. We had a coffin made and had him buried as decently as circumstances would allow. The same day had chit from Dr. Fullerton, who desired us to come over to Patna'. Campbell supplies some additional details, 'The Phousudar sent a *standing cot* for Captain Carstairs and appointed a house for his being ashore *as his wounds began to mortify and very offensive to us in the boat*. Prevailed upon him to go shore at 12; at 3, he died'. Fullerton also noted in his diary that the party which came from Hadgipore had lost Carstairs, who died of his wounds.

Fullerton met at Patna, Anderson and Campbell on 5th July, explained the position and asked them to go to Monghyr. For nearly a week, the diaries are silent with regard to anything connected with medical matters. Then on 12th July, Campbell wrote of his pain (gout). 'Upon getting up this morning, I was greatly alarmed with a violent pain in the instep of my foot; could attribute no cause for it, unless it was Dr. Anderson's head who lay just by my

feet; as it is pretty heavy it was generally believed to be the cause by lying on it . . . Later, in the day, he added 'The pain of my instep increased to a violent degree and before evening was fully satisfied that it was not owing to Dr. Anderson's head but rather appeared to be a touch of *gout* which I am very sorry for'.

On the 16th, Fullerton was sent to Monghyr. Anderson and Campbell arrived at Jaffar Khan's Garden and suffered from and wrote bitterly of, the extreme heat and the infestation by bugs and flies. On the 22nd, they were moved to a special building for state prisoners, where they had to live on restricted diet and drink. After a few days of waiting for supplies from the Governor, they sent Nicolo, their servant, to the Durbar to the Governor, on 30th July, with the following request :—'We should be glad he would order us an allowance in money for victualising ourselves. Likewise we demanded leave for some liquor'. Anderson queerly adds :—'To-day we sent to the Nabob to request that we might be allowed to send to the Dutch for a little liquor daily as the *custom has rendered it necessary for our healths*'. Both requests were granted; sanction was given for four rupees per day for victuals and two or three bottles of liquor per day. Next day, 31st July, Anderson noted with pleasure that they got a case of gin from the *Dutch Doctor* for 50 rupees. Campbell refers to the same event in a very sarcastic passage :—'Don Nicolo purchased a case of gin from *Dutch Snout's Scraper* for Rs. 50'. The Dutch doctor was a Jew. Anderson noted again on the 2nd August :—'Brought to-day six bottles of very good Madeira for three rupees per bottle'. Campbell's diary for the 3rd and 4th August, throws a sidelight on Anderson's moods and eccentric character. 'Anderson was a little out of humour this day and did not eat his dinner as usual, owing to a mistake made in describing a house that he and some gentlemen built at Neg . . . Nothing material to-day except that Anderson was highly offended with me at dinner for wanting to drink out of the cup before what he calls his allowance of gin'. Anderson has no entries on both these points. About 10th August, Fullerton was allowed to see Mr. Ellis's party, who were confined at Monghyr. He notes that he was allowed to see Mr. Ellis and party, as *Mr. Turner was ill*. Later, Turner died of *dysentery*.

It is in the entry for 11th in Anderson's diary that the details of the attack and ghastly murder of Amyatt are given. After the middle of August the diaries of Campbell and Fullerton are blank. Anderson makes an entry dated 23rd August :—'Fair and clear weather to-day which gives us great joy as the rain for these four days past has occasioned such a damp, as affects our health, *Campbell being sick*'. On the 31st again, he noted receiving some intimation from Fullerton. On 19th September, Dr. Fullerton was sent from Monghyr to Patna and

confined alone in the *killa*. He records the details of the tragedy on the 5th October, the Patna massacre, 'an outrage against humanity'. Anderson made the following poignant and prophetic entry on the 6th morning :—'Heard this morning that Mr. Ellis and 47 other gentlemen were cut off last night, so that, doubtless, our fate must be in 24 hours for which God prepare us all'. Campbell is believed to have been murdered at Chalisatoun, along with Captain Wilson and some six or seven other Englishmen.

Anderson was killed at Patna. Only Dr. Fullerton, a favourite of the Nabob, with great influence at court and powerful friends was spared. On the 7th, he had an interview with the Nabob which is described by him in the diary: Fullerton was finally permitted to stay at the Dutch factory at Patna. A week later, on the 15th, Dr. Fullerton made his escape from the Dutch factory to the camp of the English Army, which had successfully routed the native forces and arrived on the other bank of the river.

## Medical News

### THE SCHEME FOR THE CONTROL OF TUBERCULOSIS BY ORGANIZED HOME TREATMENT

It is only possible to give a brief outline of the Scheme for 'The Control of Tuberculosis by Organized Home Treatment' with an explanation of its necessity, its principles and its essential activities. This scheme was approved at a meeting of the Central Committee of the Tuberculosis Association held in New Delhi on 27th March, 1940.

#### THE NECESSITY FOR THE CAMPAIGN

Again and again it has been argued that a tuberculosis campaign in India will be useless until the hygienic and economic and social conditions have so improved that a higher standard of living becomes possible. Then it is said that tuberculosis will fade away by itself and therefore all previous efforts to prevent and treat the disease will only be waste of money and energy. But in no country in the world has tuberculosis disappeared with the raising of the standard of living. Only where there has been a vigorous attack on the disease itself by various anti-tuberculosis activities has the prevalence of the disease been reduced.

Without in any way minimizing the support the tuberculosis campaign derives from a raised standard of living it must be emphasized that a direct attack on the sources of infection is absolutely necessary to bring the disease under control. In a country like India, where a raising of the general standard of living is likely to take generations, and where tuberculosis is on the increase, it would be disastrous not to organize a campaign which would strike at the real cause of the spread of tuberculosis, the centres of infection.

#### The principles of the campaign

The principle, therefore, behind the whole campaign in India must be to search out the tuberculous patients in order to fight the disease where it exists and is spreading. But if the many and costly anti-tuberculosis measures found necessary in the West for such a campaign be compared with the meagre resources of money and personnel in India, who can wonder if administrators and others have despaired of even beginning a tuberculosis campaign in India. It is, however, a serious mistake to think that no effective campaign could be carried out in this country without transferring wholesale all the Western anti-tuberculosis measures, some of which are quite unsuitable to present Indian conditions. We can begin with those which have already proved of value in India and those which can easily be adopted and developed.

By beginning in this way it will be possible to fight tuberculosis in India by a campaign based on the right principles and to build up a balanced scheme with power enough to break the present almost unopposed onslaught of the disease. In a few years it should be possible to reach hundreds of thousands of the most

dangerous sources of infection and by helping them in their own homes prevent their spreading the disease to others.

Such a scheme of control of tuberculosis by organized home treatment is not the ideal one, but it is the only one which from a practical point of view has any prospect of success under existing conditions and for a long time to come. It is true, as has been clearly demonstrated in the West, that institutional treatment and isolation of tuberculous patients bring far better results than any home treatment, but while such measures to any great extent are for the present impossible in India, all efforts should be concentrated on a scheme which will be immensely more effective than what is at present being done. In time this will naturally be improved and developed along lines known to be the best.

Moreover, the scheme does not consist merely of ordinary treatment in the home but of prevention and 'organized' home treatment. The word 'organized' implies the application, as much as possible, of the modern specialized treatment and prevention to thousands of homes where at present patients are often left alone without any treatment whatever and without any preventive measures.

#### The essential activities

The scheme needs five main activities for its successful working, namely:—

- (a) The tuberculosis clinic.
- (b) Institutional treatment for a certain number of selected patients.
- (c) Close co-operation between the clinic and the private practitioners.
- (d) Care and after-care committees to work in connection with the clinics and other tuberculosis institutions.
- (e) Colonies or settlements for tuberculous ex-patients.

The particular importance of each of these activities in the campaign in India needs perhaps a brief explanation.

#### (a) The tuberculosis clinic

The tuberculosis clinic must have as its object prevention and, to a certain extent, treatment.

It is not necessary to go into detail about the various measures of prevention, which the clinic should introduce in the homes of patients under the supervision of the doctors treating the patients, but two measures of prevention need to be mentioned.

One is the tuberculosis survey to be conducted by the clinic. Only by this is it possible to detect many persons carrying on their work and having tubercle bacilli in their sputum; they may not know that they are sick or that they are suffering from tuberculosis. Such 'carriers' are very dangerous sources of infection to any who are in close contact with them in their offices, work-rooms, and homes. The discovery of such carriers and the diagnosis of tuberculosis is a preventive

measure of the greatest importance. In every large city in India there should be a tuberculosis clinic equipped with all modern facilities for diagnosis, and which could be a consulting institution also for the doctors in the city.

The other measure of prevention needing mention is treatment which a clinic in India must give under the present circumstances. Artificial pneumothorax may be given as an example. By introducing this treatment, and in co-operation with the private practitioners controlling its effect, a great number of patients will be helped to get better in their homes, and approximately half of them will cease to have tubercle bacilli in their sputum and so cease to be sources of infection to others.

#### (b) *Hospital wards and sanatoria*

It is now possible by certain chest operations to cure many advanced patients in whom all other treatment has failed. These operations cannot be performed in a clinic but only in a fully equipped tuberculosis hospital or sanatorium. In the scheme of control of tuberculosis by organized home treatment these institutions therefore have their place.

In or near every large city there should be such a tuberculosis institution with 100 to 200 beds, but these beds should be reserved only for patients in need of the special treatment which cannot be given in their homes or in the clinics, and after the special treatment the patients should return home for further treatment by practitioners in consultation with the clinic doctor. In this way a small number of beds can become of the greatest value and play an indispensable part in the campaign.

These tuberculosis wards and sanatoria are also of great importance for the teaching and training of doctors. Without them the doctors in the city or province would have no opportunity of learning the modern methods of treatment and prevention for application in their practice. Teaching should, therefore, be given through post-graduate courses in these institutions and in the clinics.

For the training of tuberculosis specialists each province or larger state should have a well-equipped central sanatorium with at least 200 beds. Patients should be admitted to these institutions for their whole period of treatment and not just for the time of special treatment. Apart from the value to the patients themselves it is necessary that the doctors under training should follow the treatment from beginning to end.

Only doctors who have had long training and experience in such central institutions should be placed in charge of tuberculosis wards or sanatoria. These teaching sanatoria are best situated away from large cities in good climatic conditions.

#### (c) *Co-operation between clinic doctors and private practitioners*

No anti-tuberculosis campaign anywhere in the world has succeeded without close co-operation between the clinic and the private practitioners. The private practitioner must come to understand that the clinic is his best help and if this is to be so all competition between the two must be avoided. The clinic doctor should not be allowed private practice but should be compensated in this respect. Close co-operation with the clinic will increase the reputation of the private practitioner as the public will soon discover that his patients receive better and more specialized treatment.

Special arrangements will need to be made for poor patients who cannot afford to pay any fee to the private practitioners. Unless these patients also are reached the campaign cannot succeed. The doctors who visit these patients, of whom there will be many, should have some remuneration. This should be done through a care and after-care committee in connection with the clinic. This committee should pay a small fee to the doctor who visits and treats the poor patients, but only on the recommendation of the clinic doctor. He will assure the committee that the patient is really suffering from tuberculosis, that the patient is receiving the best treatment possible under the circumstances and that

the proper preventive measures are being carried out in the home.

#### (d) *Care and after-care committees*

Besides the work of a care and after-care committee in maintaining a close connection between the clinic and the private practitioner in caring for very poor patients already mentioned, it has other important functions. Among these are helping the poor patient and his family either by food or by money, helping to isolate children from sick parents by placing them with relatives if possible or by caring for them in open-air shelters in day-time, and in finding suitable employment for patients restored sufficiently to work.

For expenditure connected with such work the committee will need a fund. When it is seen that the most effective way of distribution of help to tuberculosis patients is through such a committee working in close co-operation with the clinic and other tuberculosis institutions, it will come to be realized that the committee should receive grants from Government and local bodies as well as subscriptions from the public. Support given to such a committee is not merely a charity but is also a self-defence against the disease.

#### (e) *Colonies for tuberculosis ex-patients*

There are always a number of patients who have very little hope of being able to maintain the good results of treatment when again exposed to the strain of their old conditions. They break down and as tubercle bacilli usually reappear in their sputum, they become once more a source of danger to those among whom they live.

It is now more and more being recognized all over the world that in many patients the ultimate results of treatment depend to a great extent on the after-care, and that without this much of the expenditure of skill, time and money in treatment is wasted. In the effort to help this class of patients various after-care schemes, such as colonies for ex-patients, have been brought into being. Experience has shown that a colony for ex-patients succeeds only when linked with a sanatorium and is justified only if it develops as a part of a combined institutional scheme.

The financing of an ex-patients' colony depends, of course, on the size of the scheme, but it is not impossible to introduce such colonies in India if adapted to existing conditions. There is already evidence to show that the beginning of a colony in India can be made at a very low cost and that one may develop to be self-supporting, or nearly so, in maintenance expenditure. Such a colony should be constructed in simple village style with ordinary village houses only slightly altered to make them more open.

There are two great principles behind a colony, namely, medical help at hand for the colonists and work which gives financial security for them.

A scheme of prevention would not become fully successful without such ex-patients' colonies. They should therefore be introduced gradually in connection with each large sanatorium.

#### *Co-operation*

One of the watchwords of the whole tuberculosis campaign is education but in India it is more necessary to emphasize again and again co-operation. In the West this is a factor which now works automatically, co-operation between the tuberculosis institution and the public as well as their doctors on the one hand, and on the other between the tuberculosis institutions and Government, local bodies, and voluntary tuberculosis associations.

Co-operation is the pivot on which the whole tuberculosis campaign must turn if it is to be successful.

#### MANUFACTURE OF DRUGS IN INDIA

A list of important drugs used by the Medical Stores Department in India was prepared by the Drugs Supply Committee at its meeting in Simla. The list is to be sent to manufacturing firms in India in order that they



may investigate the possibility of manufacturing these drugs in India.

The first meeting of the Drugs Supply Committee was held to consider the question of the supply of drugs, chemicals and biological products to the Medical Stores Department. Major-General G. G. Jolly, C.B.E., K.N.R., I.M.S., Director-General of the Indian Medical Service, presided.

The Committee considered, at length, the report of a departmental committee appointed in February 1940 by the Director-General of the Indian Medical Service to investigate the sources of supply of drugs, chemical and biological products for the Medical Stores Department, the use of suitable substitutes where essential drugs were not available and measures of economy in the use of drugs during war time.

In order to assist medical officers, lists of essential drugs, chemicals and sera were drawn up giving substitutes to be used where they were not readily available. A list of British or Indian equivalents or alternatives for foreign proprietary remedies commonly used in hospitals in India was also drawn up for ready reference.

A list was also prepared of imported drugs which are expected to become progressively more expensive and difficult to obtain either through shipping difficulties, war demands or world shortage in order to warn medical officers of the necessity of restricting their use as far as possible.

### PRODUCTION OF CHEMICALS

It is expected that twelve important industrial chemicals will be in production in India by the early part of 1941. Already one plant is producing sulphuric acid from indigenous raw material; namely, Simla pyrites.

The Department of Supply have interested Indian chemical manufacturers in the production of bichromate and it is anticipated that one well-known Indian firm will be in production early next year on a scale which will enable the whole of India's normal demand to be met.

A prominent textile firm in the south of India, by far the largest individual consumer, is taking steps to instal a plant to produce its own requirements of bichromates, and it is hoped to commence production in August. A large Indian chemical firm is also importing and distributing these compounds on normal terms of business but will only sell on instructions from the Department of Supply.

This industry, which is being promoted with direct encouragement from Government, will be assured that if it is conducted on sound business lines it will be protected by Government against unfair competition from outside India.

### RECRUITS SUFFERING FROM TRACHOMA

THE increase in the percentage of rejections at recruiting centres for trachoma in the last two or three years has caused considerable concern to the Indian Soldiers' Board.

The number of rejections of candidates due to this eye disease in the Delhi area in 1937 was nine times greater than those rejected in the previous year. The figure for 1938, though less than that of 1937, was seven times the figure for 1936.

The matter was taken up with the Public Health Commissioner with the Government of India, who pointed out that the figures for the general population could not suggest any abnormal increase in the number of cases treated for trachoma in the Punjab and Delhi areas.

The increase in the number of promising young men rejected because of trachoma, however, suggests a

marked increase of the disease in the recruitable male population in the Delhi recruiting area.

The percentage of rejections at all recruiting centres in India from all causes rose from 35.73 in 1937 to 43.5 in 1939. Rejections due to trachoma made up five per cent of this total.

Next to Delhi, Jullundur recorded the largest rejections on grounds of trachoma and Ajmer and Poona the smallest.

### CHEAPER QUININE

A FIVE-YEAR programme to develop cinchona cultivation, to be taken in hand at once, has been recommended by the Advisory Board of the Imperial Council of Agricultural Research.

Rising prices and a growing scarcity of supplies, caused by the war, have made the attainment of self-sufficiency in respect of quinine a necessity for India, and to this end a plan of research has been drawn up, with the objects of increasing the output of cinchona per unit of land, and of reducing the cost to the consumer.

The plan proposes that two research stations should be set up, one in the north of India and one in the south, both to work on the same plan and not independently of each other. To each station will be attached State nurseries, and test-plots will be laid out in selected areas.

The research stations will carry out a comprehensive programme of research, involving work of a fundamental nature. The immediate object of the State nurseries will be the supply of planting material to new concerns, but ultimately it is intended to place the present empirical methods of nursery work on a scientific basis. The test-plots will be used to determine the suitability of land for growing cinchona.

It may be said that cinchona-growing in India has failed to move with the times; that it has developed as an art, rather than as a science. The early success of the grower has ultimately proved to be a misfortune, in the sense that attention was soon diverted from the more technical aspects of cultivation and utilization to the problem of large-scale production.

Mr. A. Wilson, on whose report on the prospects of cinchona-growing the proposed programme is based, suggests that India's failure to utilize modern advances in science is no doubt due to concentration on the routine of production and distribution, by an inadequate staff of workers.

This, he adds, was perhaps of no great consequence while the demand on the local industry was small, but now that the need for more adequate and cheaper supplies of cinchona alkaloids is being keenly felt an immediate change of policy is called for.

### INDIAN FISH OILS

FOLLOWING the discovery at Fanur Research Station (Madras) of four more Indian fish the oil from which has from 3 to 19 times the vitamin potency of cod-liver oil, a scheme has been prepared to popularize the manufacture of medicinal fish oil in fishing villages, as a cottage industry. The presence of vitamin A in appreciable proportions in Malabar sardine oil has been confirmed by investigations at Fanur.

Practical steps have been taken in Bombay, Madras and Bengal to develop the Indian fishing industry. In Bombay, as a result of the introduction of motor-launches to carry the catch to market, the price realized for fish has in some cases been increased from Re. 1 per thousand to Rs. 12 per thousand. There are indications that there would be considerable scope for the sale of fish if suitable marketing and transport facilities were available.

Survey work on fish marketing, under the direction of the Agricultural Marketing Adviser to the Government of India, has been started in the provinces and states.



# FOREIGN AUXILIARY TO THE NATIONAL RED CROSS SOCIETY OF CHINA

*A Survey of the West River District made by Dr. R. L. Cockfield of the United Church of Canada*

DR. COCKFIELD left Hongkong for the West River area on 27th December of last year, the purpose of his visit being:—

1. To ascertain at first hand the use to which drugs already supplied by this committee had been put.

2. To discover what further assistance is needed by the various agencies caring for refugees, sick and wounded, and in what way they could best be helped.

3. To ascertain if any large section in need of medical aid is at the present time not being served by any agency, and in what way this particular need can be met.

4. To make available such medical advice as could be given, where such was needed, and more especially where there is no doctor on the spot.

We give an account of his trip in Dr. Cockfield's own words:—

'From Macao by launch, tow-boat, sampan and walking, we reached Yan P'ing three and a half days later.

The Yan P'ing Hospital is situated on the very outskirts of the town, in buildings that were formerly used as a bus station. Very useful work has been done here in the past six months, but as Yan P'ing is now so far removed from any scene of action, and after some unfortunate experiences in removing the wounded to this hospital, the authorities finally decided that they could not send the wounded so far. It was decided to transfer part of the Yan P'ing hospital to Kung Yik. So Dr. Sporer with one nurse and four first-aid workers, are now at Kung Yik; the rest of the staff, including one Chinese doctor, are supplied by the local authorities. Dr. Sporer will return to Yan P'ing for a few days in each month to give general oversight to the work there. I called at Kung Yik on my way out and found that the hospital was already busy with both wounded civilians and soldiers.

From Yan P'ing we went to Yeung Kong, where there are two agencies for the care of the sick:—

1. The American Presbyterian Hospital, with a 50-bed capacity.

2. The American Maryknoll Mission Dispensary. Both these are doing excellent work and are quite adequate to the needs of the district.

We next retraced our steps via Yan P'ing to Sun Cheung, which is the centre of the very thickly-populated area. But there is at present no hospital or dispensary worth the name. It was decided that if he were so authorized, Dr. Sporer could fill a great need by opening and overseeing a clinic in Sun Cheung. The Foreign Auxiliary has arranged to supply the necessary drugs for this clinic at Sun Cheung.

From Sun Cheung we went to Tak Hing, on the river, three and a half days away. In Tak Hing there is a 30-bed hospital. We found a very small number of in-patients, but a rather well-attended out-patient department. Tak Hing has remained almost untouched by the war, but has many refugees, chiefly from Canton.

Next we went further up the river for about five hours to Do Sing, where we ran into a situation fortunately not frequently encountered in the West River area—a town of about 35,000 with about 10,000 refugees, where there is no organization for care of the indigent sick or wounded. Learning of a Maryknoll Mission at Wat Naam, which is about five hours inland from Do Sing, we went over for a talk with Father Rauschenbach, who is well aware of the situation at Do Sing and would be glad to furnish the necessary trained dispenser and personnel over-sight if he can get the drugs and a centrally-situated shop for dispensary. The Foreign Auxiliary has therefore granted to Father Rauschenbach the sum of N.C. \$36 per month for a minimum of six months for rent of a shop, as well as the necessary drugs for the relief of indigent sick and wounded in Do Sing.

At Wat Naam itself the Maryknoll Mission runs the only free dispensary under Dr. Rauschenbach, as well as two others in the surrounding country. Wat Naam has a population of about 20,000 and harbours a great many Canton refugees.

Our next visit was to Wuchow. This city has suffered the most from air-raids of any city which we have seen. However, in spite of the repeated bombings, the city is well populated, but has a large number of desperately poor, who require more than ever before the ministrations of the various medical agencies now at work here. The Stout Memorial Hospital, under the American Baptist Mission, has a 40-bed capacity and is fully staffed and equipped. At present it is receiving N.C. \$50 per month from the International Red Cross of Canton for the care of sick and wounded and refugees. Some quinine has also been received from them, but this is now almost used up. The Maryknoll Mission also maintains a very good dispensary here, with French Canadian sisters in charge, who are qualified in dispensing. This mission is also the centre for seven dispensaries in the district farther up the river, all in the charge of qualified dispensers. The Municipal Hospital at Wuchow we found to be the best staffed and equipped yet encountered in South China.

The Military Hospital is just outside the city and has a 2,000-bed capacity. Nearly all the cases at present are medical, chiefly malarial and dysenteric. The place is well and efficiently run, but lacks supplies of drugs. We suggested that, rather than allow the patients to suffer because of these deficiencies, the Stout Memorial Hospital should supply them with urgently needed drugs from their own stock and that this committee should make good any such contributions. The Foreign Auxiliary has agreed to supply these extra drugs.

From Wuchow we went by tow-boat down the West River to Lok To, eight hours away, and then inland to Wan Fou, where there is a small dispensary of the Maryknoll Mission, which is quite adequate to the needs of the 15,000 inhabitants.

Thence we went further inland to Sun Hing, which is a large town of 50,000 inhabitants, where there is a poorly equipped and poorly staffed Municipal Hospital, not adequate to the needs of a town which has suffered badly from bombing. A dispensary will fill a real need here, so we approached the Southern Baptist Mission with this problem and they will supply the necessary dispenser and premises for the dispensary, if the Foreign Auxiliary will supply the drugs.

As a result of my experiences I made the following observations:—

1. The drugs already supplied, chiefly quinine, have saved thousands of lives and relieved an unassessable amount of suffering. They have been dispensed with extreme caution, my only criticism being that, if anything, they were being too careful, especially with the quinine. All the dispensers are well qualified to diagnose simple ailments and supply the required drugs.

2. The diseases most commonly encountered, in order of frequency, are:—

Malaria, intestinal parasites, chiefly round-worm and hook-worm, typhoid, dysentery, mostly amoebic, skin diseases, eye troubles, mostly trachoma, chest cases, tuberculous and others, Bright's disease, massive oedema, smallpox, at present epidemic in some places, beri-beri, mostly among the soldiers, general mal-nutrition, prevalent all over the district.

3. Although one can scarcely imagine such a large area ever having a really adequate medical service even in normal times, one is impressed by the tremendous amount of really good medical work being done. Given support, the agencies already existing, with one or two additions, can and will fulfil a vital function in the provision of medical service to the sick and wounded. This support must be forthcoming if they are to continue this work, as unprecedented demands are being made on their resources, which they cannot meet without our help.

The Foreign Auxiliary has undertaken to supply drugs to the value of H.K. \$10,239.60 to the West River District, in addition to a total of 1,000,000 tablets of quinine for the next six months.

#### *Our appeal*

These drugs will help the wounded sick and civilians and refugees in the West River District to regain health and to become once more useful citizens of the New China. But the Foreign Auxiliary needs funds to renew stocks, which are becoming sadly depleted at a time when it is absolutely essential to continue supplies to every distressed area in China.

[Note.—Messrs. Thacker's Press and Directories Limited, the proprietors of the *Indian Medical Gazette*, are sending a donation to this worthy cause and will be pleased to transmit any sums sent to them by our readers, in response to this appeal.—Editor, *I. M. G.*]

### THE PHARMACEUTICAL AND ALLIED MANUFACTURERS' AND DISTRIBUTORS' ASSOCIATION, LIMITED

We have received a copy of the Memorandum of Association and Articles of Association of the Pharmaceutical and Allied Manufacturers' and Distributors' Association, Limited, recently formed in Bombay. The seven members represent some of the principal drug distributing agencies in Bombay and in our opinion this association cannot fail to be of great assistance to the drug trade in Bombay in particular and it will have a wide sphere of influence, as a properly constituted body of this nature will have much greater power in influencing Government in the interests of drug manufacture and distribution than isolated firms would have. It is a move in the right direction and a step in improving drug distribution in India and we wish it all the success it deserves.

### EMERGENCY COMMISSIONS—INDIAN MEDICAL SERVICE

In view of the many applications received for emergency commissions in the Indian Medical Service from medical men who fulfil all the conditions for the grant of such commissions except that they are over age, the Government of India have decided to grant the Selection Board powers to relax the age limit up to 40 years of age in the case of candidates suitable in all other respects.

Medical men above the former maximum age limit of 32 and up to 40 years of age will be eligible for commissions on the same terms as younger men, that is to say, on selection they will be given the pay and allowances admissible to short service commissioned officers in the regular cadre of the Indian Medical Service and on release after the war will receive a gratuity at the rate of one month's pay for every 12 months' service. They will also be eligible for disability pensions, while widows' and other dependents' allowances will be admissible under the same conditions as for permanent officers of the Service.

While during the war Government are accepting no new commitments as to the grant of permanent commissions, selection for appointment to permanent vacancies in the Service will on the conclusion of the war be made from among all officers holding emergency commissions.

Emergency commissions only are being granted during the war. Selection for commissions will be made on the recommendation of the Indian Medical Service Selection Board from amongst candidates who apply to the Director-General, Indian Medical Service, Simla, for appointment.

### INDIAN MEDICAL BIRTHDAY HONOURS, 1940

The following are the names of medical men and others associated with medical institutions in the Indian

Honours List of date 11th July, 1940. We offer them our congratulations:—

#### *C.I.E.*

Colonel (Honorary Brigadier) H. C. Dibben (Retired list), lately Director of Veterinary Services in India.

#### *Khan Bahadur*

Syed G. Hussain Sahib Bahadur, Civil Surgeon (Retired), Madras.

#### *Rai Bahadur*

Rai Sahib H. Singh, District Medical Officer of Health, Lahore, Punjab.

Rai Sahib S. Pujari, Professor of Anatomy, Prince of Wales Medical College, Patna, Bihar.

Mr. N. Ghosh, Teacher, Berry-White Medical School, Dibrugarh, Assam.

#### *Rao Bahadur*

Mr. R. A. G. Ayyar, District Medical Officer (Retired), Madras.

Mr. N. R. Summanwar, Civil Surgeon, Wardha, Central Provinces and Berar.

#### *Shifa-ul-Mulk*

Hakim M. N. Zahiri, Member, Board of Indian Medicine, Meerut, United Provinces.

Hakim M. H. Qarshi, Principal, Tibbia College, Lahore, Punjab.

#### *Khan Sahib*

Syed R. Hussain, Medical Officer in Sub-charge, Bulrampur Hospital, Lucknow, United Provinces.

Mr. C. M. Ahmad, Hospital Surgeon, Punjab Veterinary College, Lahore, Punjab.

Maulavi M. A. Hai, Lecturer in Pharmacology, Prince of Wales Medical College, Patna, Bihar.

Jemadar G. Muhammad, in charge, Swat State Hospital, North-West Frontier Province.

#### *Rai Sahib*

Mr. K. Prasad, Medical Officer in charge, Health Unit, Partabgarh, United Provinces.

Mr. D. Chand, Sub-Assistant Surgeon, Civil Hospital, Allanmyo, Burma.

Babu L. Ram, Assistant Surgeon, Sadar Hospital, Ranchi, Bihar.

Babu J. N. Sen, Assistant Surgeon, Sub-divisional Hospital, Dhanbad, Bihar.

#### *Rao Sahib*

Mr. H. N. A. C. Ayyangar, Lecturer in Anatomy, Madras Veterinary College, Madras.

Mr. A. S. Barot, Medical Practitioner, Dohad, Broach and Panch Mahals District, Bombay.

Mr. P. A. Patadia, Medical Practitioner, Wadhwan Civil Station, Western India State Agency.

## Current Topics

### The Therapy of Dropsy

By H. M. MARVIN, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXIV, 2nd March, 1940, p. 757)

Dropsy, or œdema, is usually defined as the accumulation of serous fluid in the intercellular spaces of the subcutaneous or deeper tissues and in the serous cavities. The source of this fluid is the blood, from which it has escaped by passage through the walls of the blood vessels. Œdema is always but one manifestation—although sometimes the most dramatic and important—of some abnormality or disease process, and its removal by medical means should logically begin with treatment of the causative process. Specific

measures for its removal are necessary only if its location or extent render it harmful or uncomfortable to the patient and should ordinarily be employed only after correction or treatment of the underlying abnormality.

There are many conditions with which oedema may be associated, but only a few of these will be considered in this review, which is concerned primarily with the practical aspects of medical treatment. The conditions to which attention will be devoted comprise congestive heart failure, acute and chronic nephritis, cirrhosis of the liver, the Pick syndrome of constrictive pericarditis, vitamin deficiency and marked lowering of the protein content of the blood plasma, whether this is found in malnutrition, in chronic glomerulonephritis or in so-called lipid nephrosis.

For a clearer understanding of the discussion that follows, it is desirable to review briefly the mechanisms involved in the formation of oedema. The opinion first expressed clearly by Starling in 1896 has received the almost unanimous support of investigators in recent years; in its simplest form it may be stated as follows: The capillary wall is a membrane freely permeable to water and to most of the crystalloids of the blood, such as salt, sugar and urea, which pass from the capillary into the surrounding tissue spaces, or from these spaces into the capillary, in response to physical laws now well understood. The most important factor causing movement of fluid out of the capillary is the pressure exerted on it; in other words, the intracapillary blood pressure. If this were unopposed, most of the fluid of the blood would readily pass into the tissue spaces. But it is opposed, as Starling first showed, by a force due to presence of proteins, chiefly albumin, in the blood plasma. These protein substances cannot pass readily through the capillary wall; by remaining within the lumen they attract fluid powerfully through the process of osmosis, the force so exerted being known as the colloid osmotic pressure of the plasma. Obviously the direction and extent of movement of fluid through the capillary wall must depend on the balance of these two opposed forces; if the intracapillary pressure is higher than the colloid osmotic pressure, fluid will pass out of the blood stream and oedema will form. On the contrary, a rise in the colloid osmotic pressure above the capillary blood pressure will result in prompt withdrawal of fluid from the tissue spaces into the blood.

It is thought that both these processes are operating continuously in health and in disease. It is impossible to assign any constant value for the capillary blood pressure, since this varies in different parts of the body and in response to many influences, but in the capillaries at the base of the finger nail Landis has found that the pressure at the arterial end of the loop averages about 43.5 cm. of water, while the colloid osmotic pressure is about 34 cm. of water. The result of this difference is to force fluid from the capillary. But when the blood reaches the venous end of the loop the pressure has fallen to an average value of 16.8 cm., while the colloid osmotic pressure has risen because of increased concentration due to loss of water. At the venous end of the capillary, then, fluid will be drawn from the tissue spaces into the blood. It is therefore clear that oedema may result from either or both of two changes: an increase in the capillary pressure or a decrease in the amount of protein in the blood plasma.

This statement has been purposely simplified and abbreviated but is essentially correct. The mechanism that it describes is not the only one concerned in the formation of oedema but is generally regarded as the most important. The other primary and contributory factors have been lucidly reviewed by Landis, whose studies of the capillary circulation have added greatly to our knowledge. He regards as other primary factors injury to the capillary wall, which increases its permeability and obstruction to lymph channels. As contributory factors he mentions low tissue pressure, high salt intake, high fluid intake, a warm environment and disturbances of innervation. It is well to emphasize that the contributory factors may become of great

importance and may actually determine the occurrence or disappearance of oedema.

Thus in the capillary bed there are two important and opposed physiologic processes involved in the formation of oedema; similarly in the kidney there are two fundamental and opposed processes involved in the formation of urine. It is now believed that the renal glomerulus acts essentially as a filter; relatively enormous quantities of a protein-free ultrafiltrate normally pass through it into the tubules, where most of it is reabsorbed, leaving only a small percentage to be excreted as urine. It is apparent that the volume of urine may be increased by either or both of two processes: an increase in glomerular filtration or a decrease in tubular reabsorption.

With this brief outline of the more important mechanisms in mind, we may consider the treatment of oedema associated with various clinical conditions.

#### CONGESTIVE HEART FAILURE

Congestive heart failure is the most frequent cause of oedema sufficient to require treatment; fortunately it is also the condition in which specific treatment is most gratifying. The oedema is thought to be due to several factors, which probably vary in relative importance in different cases. The effective filtration pressure in the capillaries is increased by the rise in general venous pressure that occurs in congestive heart failure and also by the muscular inactivity that generally accompanies it. In addition there is increased permeability of the capillaries to water and crystalloids, and in some cases there is a fall in the effective colloid osmotic pressure of the plasma because some protein passes into the tissue spaces. The hypoproteinemia is probably increased at times by the loss of albumin in the urine and by the low protein diet often prescribed by the physician.

A detailed discussion of the treatment of congestive heart failure is beyond the scope of this article, but it is now generally agreed that this should include complete rest in bed, necessary sedatives, limitation of fluid and of salt intake, and full digitalization. These measures should precede the use of diuretics in most instances, since they will often result in marked diuresis and render further treatment unnecessary. But there are several important exceptions to this statement. If there is considerable fluid in one or both pleural cavities it should be withdrawn at once by means of paracentesis, for such fluid often causes great respiratory discomfort and is but slowly absorbed and excreted, even when diuretics are employed. Furthermore, if the oedema elsewhere is so extreme as to be the cause of danger or grave discomfort, the mercurial diuretics should be administered at once, without waiting for the effect of digitalis. I am in agreement with Thomson that the diuretic effect of these agents is often just as great without digitalis as with it, and the patient may be spared some days of discomfort if they are used immediately.

*Xanthines.*—Until about fifteen years ago the xanthine diuretics, sometimes known as the purine bases, were the only ones in general use. For practical clinical purposes this group may be regarded as consisting of theophylline and theobromine with their derivatives; caffeine is also a member but has little or no value as a diuretic in disease states. Theophylline may be administered in gelatin capsules containing from 3 to 5 grains (0.2 to 0.325 gm.) and may be given two or three times a day. Even in this small dosage, however, it often causes nausea and vomiting after four or five doses have been given and must then be discontinued. Because of the likelihood of vomiting, it is usually wise to give theophylline for periods of only a few days at a time, even if it is well tolerated; there is some evidence that the total diuretic effect is greater with intermittent than with continuous administration. It is the most potent of the xanthine diuretics but can seldom be given in effective dosage because of its unfortunate side actions. In recent years it has been used far more frequently in combination with other salts, the best known preparations being theophylline with sodium acetate and theophylline with

ethylenediamine (aminophylline). These are usually tolerated better than is theophylline alone and can therefore be used for longer periods, but it is well to omit them for a few days after a period of brisk diuresis. Theophylline with sodium acetate is available in tablets containing from  $2\frac{1}{2}$  to  $7\frac{1}{2}$  grains (0.16 to 0.5 gm.); those which have an enteric coating are better tolerated by most patients. The therapeutic dose should be determined in each case by actual trial, starting with small amounts in order to avoid the induction of vomiting. Total daily quantities of from 15 to 30 grains (1 to 2 gm.) can be taken by many subjects without discomfort if given in three or four doses, but amounts less than this often cause satisfactory diuresis. The other preparation, theophylline with ethylene diamine, is better known to-day because of its widespread use in recent years for its supposed effect on the coronary arteries. It is not a potent diuretic but may be of value in preventing the reaccumulation of oedema that has been successfully removed by other agents. It is marketed in tablets containing  $1\frac{1}{2}$  grains (0.1 gm.), and six or eight of these a day are required in most cases for any significant diuretic effect. Like other theophylline preparations, this also may cause nausea if given in doses sufficiently large to increase the volume of urine.

The Council on Pharmacy and Chemistry makes the following statement concerning the actions and uses of xanthine derivatives:—

*Actions and uses.*—The Council recognizes no therapeutic claim for any xanthine derivative beyond those for diuretic action and for use as a myocardial stimulant. Theobromine and theophylline surpass caffeine in their diuretic, and perhaps in cardiac and muscular actions. They are therefore generally preferred in cardiac oedemas, etc., since they are equally, or more, effective, more prompt and largely avoid the unpleasant side effects (insomnia, nervousness, gastric disturbance) which often interfere with the use of caffeine in adequate doses. This freedom from side effects holds true, particularly for theobromine. Theophylline surpasses theobromine in diuretic efficacy, but its action is probably not so lasting; it may produce gastric disturbances; renal irritation has been reported. Theobromine is therefore generally preferred, sometimes preceded for a few days by theophylline. If central stimulation is desired, caffeine must be used.

It has been the experience of almost all observers that theobromine and its compounds are less powerful diuretics than the closely related substances just named, but they are often well tolerated in effective dosage and may therefore prove to be far more satisfactory. Theobromine may be administered in capsules in doses of 5 or 10 grains (0.325 or 0.650 gm.) three times a day and continued for a number of days if nausea does not occur. One of its best known compounds is theobromine with sodium salicylate, which contains approximately 50 per cent theobromine. This is one of the mildest of all diuretics, seldom causes nausea or vomiting and must be given in doses of from 40 to 60 grains (2.6 to 4 gm.) or more a day. Another preparation is theobromine calcium salicylate, or theocalcin, which is said to contain 48 per cent theobromine, 11 per cent calcium and 38 per cent salicylic acid. Stewart's study indicated its advantages, and these have been confirmed by subsequent experience. It is a potent diuretic, often superior to theophylline in this respect, seldom causes nausea and may be continued without intermission as long as diuresis results. It is available in tablets containing  $7\frac{1}{2}$  grains (0.5 gm.), and the usual effective dose is from three to six tablets a day; larger amounts may be given if necessary.

It is the belief of many students that the xanthines cause diuresis by an action on the renal glomerulus, increasing the infiltration, but authoritative opinion is not agreed on this.

The xanthines as a group are far from negligible; in recent years they have been overshadowed and to a large extent superseded by the mercurials, but they have an important place in the treatment of patients

with slight or moderate oedema and of those patients who object seriously to intravenous injections.

*Organic mercurials.*—The mercurial diuretics are unquestionably the most effective available to-day, even though an occasional patient may exhibit a greater response to one of the xanthines. Merbaphen, the first to be introduced, has been almost completely displaced in recent years by salyrgan, which is regarded as more potent and less toxic. These are organic mercurial compounds containing about 10 per cent of mercury and are effective when administered by intravenous or intramuscular injection or in the form of rectal suppositories. Their effectiveness is greatly increased if acid-producing salts are administered by mouth for several days preceding the injection, and this preliminary medication should be a routine unless the need for the first injection is urgent. Ammonium chloride and ammonium nitrate are the salts most commonly used, but calcium chloride and calcium nitrate are also effective. It has been shown that there is a true synergism between these salts and the mercurial preparation; all four regularly cause a lowering of the carbon dioxide combining power of the plasma and increase the diuretic response. Alkalinizing salts cause a rise in the carbon dioxide combining power and a decrease in the diuretic effect, while neutral salts cause no change in either function. The statement is often made that doses of these acid-producing salts as large as from 90 to 120 grains (6 to 8 gm.) a day must be given in order to secure satisfactory results, but my experience is in accord with that of Thomson, who has found doses of from 60 to 90 grains (4 to 6 gm.) quite sufficient. Even these smaller doses will almost invariably cause nausea and vomiting unless administered in the form of enteric coated tablets, which are taken by most patients without discomfort in the doses mentioned.

The mercurials for injection are available in ampoules containing 1 and 2 c.c. It is customary to give only from 0.5 to 0.75 c.c. at the first injection, in case there should be an idiosyncrasy to mercury or some untoward reaction, both of which are rare. Subsequent doses are usually 2 c.c. If the patient requires a series of injections it is satisfactory to continue ammonium chloride without interruption and inject the mercurial every third, fourth or fifth day. The results are almost always satisfactory and sometimes astonishing; it is not unusual to secure a urinary secretion of from 6 to 10 litres in twenty-four hours, and quantities as large as 15 or 16 litres have been recorded.

A few years ago Shelling and Tarr reported that the diuretic effect of salyrgan might be increased by combining magnesium sulphate with it. They recommended the use of 15 c.c. of 50 per cent magnesium sulphate with 2 c.c. of salyrgan and 1.5 c.c. of 5 per cent procaine hydrochloride, the whole to be mixed thoroughly in a 20 c.c. syringe and injected deeply into the gluteal muscles. There can be no question that this combination is sometimes remarkably efficacious with patients who have shown little or no response to salyrgan alone. To secure such effects, however, it is not always necessary to use such large quantities of magnesium sulphate; a mixture of 2 c.c. of salyrgan, 6 or 8 c.c. of 50 per cent magnesium sulphate and 2 c.c. of 1 per cent procaine hydrochloride solution has often given excellent results. This is about half the total quantity recommended by Shelling and Tarr, and its injection into the muscles seldom causes pain at the time or later. It should be added that the anterior muscles of the thighs are more suitable for such injections than are the gluteal muscles if the patient is confined to bed.

It is generally agreed that the mercurial diuretics owe their effect largely, if not exclusively, to a direct action on the renal tubules, diminishing their power of reabsorption.

Since there was a widespread belief that the xanthines caused diuresis chiefly by increasing glomerular filtration and the mercurials by diminishing tubular reabsorption, it was but natural that attempts should be made to secure a more effective diuretic agent by combining the two substances. In Europe such a combination was introduced as early as 1929; several years



later it appeared in America under the name mercurpurin. According to the revised supplement to New and Non-official Remedies 1939, it contains 10 per cent of the mercurial component and 4.86 per cent of anhydrous theophylline; each cubic centimetre contains about 39 mg. of mercury in nonionizable form. DeGraff and his collaborators in a series of important studies have shown that the addition of theophylline to a mercurial diuretic causes much more rapid absorption from the site of intramuscular injection and also renders it far less injurious to the tissues. Comparative clinical studies have shown that the combination of the two substances is a more potent diuretic than is the mercurial alone, and this increased potency is apparently due entirely to the addition of theophylline. The advantages of combining the two have been so apparent in recent years that practically all mercurials now marketed in Europe have been modified by the addition of 5 per cent theophylline. Several years ago salyrgan was thus modified and is available under the name salyrgan-theophylline; apparently its content of mercury and of theophylline is approximately the same as that of mercurpurin. More recently there has been introduced a combination of the two under the name esidrone, which is said to contain 31.2 per cent mercury in nonionizable form and 28 per cent theophylline, which is chemically connected with the mercury molecule. The reports on its clinical use thus far available are not sufficient to determine whether the great increase in the amount of theophylline in the mixture has caused any considerable increase in its diuretic potency.

There can be no question that the combination of a mercurial with theophylline is the most powerful diuretic agent now available for most patients with congestive heart failure.

Both salyrgan and the mercurial component of mercurpurin are available in the form of rectal suppositories, each containing approximately 0.5 gm. of mercury and a small amount of local anæsthetic to prevent rectal irritation. A cleansing enema usually precedes the insertion of the suppository, and the diuretic response is often increased by the preceding administration of the acid-producing salts. Some observers have found the suppositories to be almost as effective as intravenous or intramuscular injections of the mercurials, but most regard them as about one-third to one-half as effective. (It should be noted that the suppositories of salyrgan have recently been found to result in rectal irritation or ulceration in so many cases that their acceptance has been rescinded by the Council on Pharmacy and Chemistry, and many clinicians have discontinued their use.) Similar unfortunate results have apparently not followed the use of mercurin suppositories, but any such preparation should be used with great caution and should be discontinued immediately on the appearance of signs of local irritation.

There is general agreement that the mercurials should not be used in the presence of acute nephritis or ulcerative colitis. For some years fear was expressed that they might cause serious injury to the renal tubules, and a few such instances have in fact been reported. But the accumulated experience of the past ten years justifies the statement that the mercurial diuretics, especially those combined with theophylline, are safe and highly effective and often retain their full potency after hundreds of injections over a period of many months or years. In the great majority of cases, even of chronic nephritis, there is no evidence that the kidneys have been injured by the mercury.

**Potassium salts.**—According to Keith and Binger, potassium salts were recommended for the treatment of dropsy as early as 1679. In recent years most of the studies relating to their diuretic action have been concerned with nephritic patients, but in 1932 Barker reported excellent results from the administration of potassium chloride to a group of patients whose cedema was due to congestive heart failure. He emphasized the importance of placing such patients on a full general diet with an excess of acid ash in which a low ratio of sodium to potassium is maintained. The dose of

potassium chloride found to be effective in most of his cases was 5 gm. (75 grains) a day; this amount was given to the patient each morning in a salt shaker and sprinkled on the food instead of sodium chloride. At the end of the day any salt remaining was dissolved in water and taken by mouth. Twelve of his sixteen patients obtained excellent results, and he observed, as others had done, that no ill effects followed even if very large doses were given for long periods.

In a later and more elaborate study, Keith and Binger found that potassium salts gave 'very satisfactory diuretic results' in 48 per cent of their sixty cases and fair results in another 33 per cent, but their figures do not indicate in how many of these cedema was due to heart failure. After a careful study of five potassium salts they concluded that the nitrate was preferable, since it frequently caused diuresis and seldom gave rise to untoward effects. They pointed out that any potassium salt must be given in large doses, amounting to 12.5 gm. or more of the nitrate a day, but state that smaller doses should be administered first. One of their patients took 24.5 gm. of potassium salts daily for thirteen days and 871 gm. in sixty-eight days without complaints or toxic symptoms! The salts may be administered in powder form or in solution, but the most satisfactory method is by means of enteric coated tablets containing  $7\frac{1}{2}$  grains (0.5 gm.) each. Like ammonium chloride and ammonium nitrate, the potassium salts may be used in conjunction with other diuretics to enhance the action of the latter.

A great many studies are in complete harmony in indicating that in the experimental animal, in normal human subjects and in patients with cedema due to several different causes the replacement of sodium by potassium results in increased excretion of water, while the substitution of sodium for potassium results in increased retention of water. The exact mechanism responsible for these results, however, is not entirely clear. It is known that potassium is quickly absorbed from the intestine and is promptly excreted by the kidney, which is able to concentrate it as much as fifty times; even after large doses the amount in the blood is seldom elevated appreciably and often not at all. In fact the careful measurements of Barker revealed practically no changes in the sodium, potassium, calcium, carbon dioxide combining power, pH, or cholesterol of the blood during the administration of potassium. In some cases it seems possible that the diuresis is linked with a shift in the acid-base equilibrium, but this cannot be demonstrated regularly.

**Bismuth.**—Ten years ago, Mehrtens and Hanzlik brought forward evidence indicating that certain bismuth preparations injected intramuscularly in small doses act as a diuretic and are almost devoid of toxic manifestations.

The reports on this preparation were so encouraging that it is surprising not to encounter further reports in recent medical literature. Untoward actions or toxic effects cannot explain this apparent neglect, for these are absent or negligible; in fact, Hanzlik states that the group of observers at Stanford University has used bismuth preparations in various ways in several thousand cases and in animals in the past twelve years without serious disturbances, injuries or fatalities. It seems probable that this drug, like others of undoubted merit, has failed to come into general use because the mercurial diuretics are usually more potent, even though their action is less sustained than that of bismuth.

According to Stockton, bismuth sodium tartrate probably causes diuresis by general tissue action, resulting in mobilization of chlorides and water. He explains the effect of the mercurial diuretics and of theophylline in the same way, whereas most students to-day believe that these substances act directly on the kidney. A belief in general tissue action of diuretics was widespread ten years ago but has been largely abandoned in the light of recent studies.

**Urea.**—Although urea has been recommended as a diuretic in renal disease for a long time, its use for the treatment of cardiac cedema seems to date from the report of Crawford and McIntosh in 1923. They found it to be of great value in seven of eight cases in

which œdema was due to heart failure and recommended it both for the removal of œdema and to prevent its recurrence. No toxic effects were observed. In 1932 Miller and Feldman emphasized several of the cardinal virtues of this substance, demonstrating that its diuretic potency does not diminish during months or years of practically uninterrupted use, that there are no demonstrable deleterious effects on the kidneys or other tissues and that it acts, alone or in conjunction with other agents, as an admirable prophylactic to prevent the recurrence of œdema.

Large doses are required, varying from 15 to 60 gm. or more (225 to 900 grains) a day. It is administered most satisfactorily in ice cold aqueous solution three times a day immediately after meals. Its unpleasant taste, which is practically its only disadvantage, can be mitigated for some patients by dissolving it in syrups or fruit juices. Syrup of acacia has been especially recommended as a vehicle for urea, its colloidal nature serving to mask the urea quite satisfactorily. Urea is rapidly absorbed from the intestine and is practically devoid of action in the tissues, even in large doses. After it has been taken for a few days the blood nitrogen should be determined to ascertain whether it is being properly excreted. In almost all instances of congestive heart failure, and even of nephritis and nephrosis, it is readily excreted and carries with it large quantities of water. This mechanical diuretic action is thought to be enhanced by decreased reabsorption in the renal tubules.

Urea is an extremely valuable diuretic and deserves wider popularity than it seems to enjoy at present. All available clinical reports emphasize its complete freedom from untoward actions and its extraordinary constancy of diuretic effect. While it is usually less dramatic in its immediate results than are the mercurials, it has obvious advantages and may be used to supplement the latter. There are but few patients who cannot take it for at least several weeks at a time, and many continue it for months or years without interruption.

#### NEPHROSIS

Despite the enormous literature devoted to the subject of nephrosis in the past thirty-five years, there is not yet complete agreement among authoritative observers as to the existence of 'pure' or 'lipoid' nephrosis as a separate disease entity. There is, however, general agreement that the combination of low serum proteins, profuse albuminuria, normal blood nitrogen and œdema may properly be known as the 'nephrotic syndrome' and that its treatment is the same whether it is regarded as resulting from a specific renal lesion, a nonspecific renal lesion (one stage in the development of chronic glomerulonephritis) or a general metabolic disease. The œdema is thought to be due in large measure, as Epstein first pointed out, to the marked hypoproteinemia, which results in great lowering of the colloid osmotic pressure of the blood.

The general principles of treatment include maintenance of the nutrition at the highest possible level by an adequate diet high in protein, limitation of salt and fluid intake and exercise in moderation as long as the clinical state permits. Practically all known diuretics have been tried in this condition; any of them may give satisfactory results in a given case but most of them prove quite ineffective. Thyroid has been extensively used because of the low basal rate in most patients but is seldom effective in causing diuresis, possibly because the low metabolic rate is caused in most instances by the undernutrition rather than by thyroid deficiency. The xanthine diuretics have proved useless in the hands of most observers. Encouraging results have sometimes been obtained from the use of potassium salts, as already outlined. Urea also has occasionally been effective in doses of from 15 to 50 gm. or more a day and deserves a trial if it is tolerated. But there can be little question that the mercurial diuretics are much the most effective in the majority of cases, and they may be used without fear of increasing the renal lesion. They should be preceded by one of the acid-producing salts. In many cases the mercurials also are useless.

Because of the belief that the œdema is due largely or wholly to the reduction of serum proteins, many attempts have been made to raise these to normal levels by means of diets high in protein and by the intravenous injection of such substances as whole blood, blood plasma and solutions of acacia. Leiter has stated that this form of treatment, however plausible it may seem, is inevitably doomed to failure because the amount of material injected cannot be sufficient to cause an appreciable increase in the colloid osmotic pressure of the plasma and because it will be rapidly excreted from the circulation, since the glomeruli are much more permeable to colloids than normally. However, Hartmann and his collaborators, Lepore, Landis and Shelburne have all reported excellent results from the repeated and cautious intravenous injection of acacia solutions. The strength of the solutions has usually been from 6 to 15 per cent, in water or in physiologic solution of sodium chloride, and the injections may be given daily or at intervals of from two to four days. In practically all reported cases of benefit from acacia many diuretics had been tried without success. Following the disappearance of œdema, a diet high in protein should be continued; Shelburne regards this as an essential part of the treatment.

The administration of acacia is not wholly without disadvantages, and some have stated that these are so serious as to make the use of the substance unjustified. The work of Dick is often quoted in support of this belief, but Shelburne has recently pointed out that this work is open to serious criticism and should not prevent the proper use of a valuable therapeutic agent. Immediate reactions to injections of acacia are infrequent if the solutions are freshly and carefully prepared, but serious reactions have followed the use of impure solutions. It seems clear that if acacia is to be used it should be in a hospital rather than in the patient's home. If other methods of treatment have been tried without success and the removal of œdema is highly desirable, recent experience would certainly justify the trial of acacia. If this also proves ineffective, other diuretics should be employed immediately after the acacia, as they may then prove beneficial.

#### VITAMIN DEFICIENCY

In the past several years evidence has been presented, chiefly by Weiss and his collaborators, indicating that deficiency of vitamins, especially of vitamin B<sub>1</sub>, may lead to various types of cardiovascular dysfunction, whether the heart was previously normal or diseased. The cardiovascular manifestations do not form a fixed clinical syndrome but may include the characteristic signs of congestive heart failure with marked œdema. The diagnosis of the condition may be very difficult, but the possibility of vitamin deficiency should be seriously considered when any patient with an abnormal nutritional history develops the syndrome of heart failure with œdema in the absence of convincing signs of heart disease. The presence of other signs of vitamin-B<sub>1</sub> deficiency, especially polyneuritis, glossitis and cutaneous changes suggestive of pellagra, may give an important clue. According to Strauss 'it is rare to observe "beri-beri heart" without at least minimal signs of polyneuritis'. Both Weiss and Strauss emphasize the possible importance of measurements of the circulatory velocity and the minute volume output of the heart, as these are increased in the condition now under discussion and are conspicuously slowed in heart failure due to other causes. The response to specific therapy, however, may provide the first and most convincing evidence of the nature of the condition.

General, or nonspecific, treatment consists of the application of the measures enumerated previously: rest in bed, limitation of fluids and of salt and the administration of digitalis and diuretics. Some patients respond well to such a regimen, while others show little or no improvement; indeed, some of Weiss's patients became worse when placed at rest. Specific treatment consists of the administration of vitamin B<sub>1</sub>. Preferably this should begin with the intravenous or intramuscular injection of from 20 to 50 mg. of thiamin chloride



daily, and this method should be employed as a routine in the more severe cases. After improvement has occurred, usually within two weeks, the dose may be decreased to 10 or 20 mg. daily, or the larger doses may be given by mouth. If the symptoms are not particularly severe or have been largely relieved by intensive treatment, brewers' yeast may be used instead of the crystalline form of the vitamin; doses of about 30 gm. three times a day are recommended.

The response to such treatment may be prompt and spectacular, with marked improvement in a few days and complete disappearance of symptoms and signs within two or three weeks, or improvement may be gradual over a period of six or more weeks. Rapid improvement is said to be associated with diuresis, slowing of the heart rate and rise in the arterial pressure. If there is not clear evidence of improvement after adequate dosage of vitamin B<sub>1</sub> for several weeks it is probable that the cardiovascular manifestations are not due to vitamin deficiency. Beneficial effects do not follow the administration of this vitamin to patients with other types of heart failure.

Weiss has properly emphasized that deficiencies are seldom limited to a single vitamin, and these patients often present evidences of inadequate intake of vitamin A and of ascorbic (cevitamic) acid, of anemia, of hypoproteinemia and possibly of other dietary deficiencies. These should, of course, receive appropriate treatment simultaneously.

#### MALNUTRITION

The oedema, often very extensive, associated with serious degrees of malnutrition is thought to be dependent in large part on the diminished proteins of the blood plasma and the consequent lowering of the colloid osmotic pressure. It is clear that this condition may be intimately related to and complicated by the vitamin deficiency state just discussed. Diuretics may be employed, but the logical and highly effective treatment is the correction of the nutritional state by means of a proper diet rich in proteins and in vitamins. Unless the patient is dying, the dropsy usually disappears with gratifying promptness.

#### PICK'S DISEASE

For many years the term 'Pick's disease' was used loosely and inaccurately and was applied to a number of quite different pathologic states. Now, thanks largely to the clinical reports of White and the experimental and surgical studies of Beck, it is possible to say with conviction that Pick's disease is actually chronic constrictive pericarditis. Among the more important clinical features of the condition may be mentioned gradual onset of dropsy, disproportionate enlargement of the liver and ascites, increased venous pressure, low arterial pressure and a heart that is normal in size or smaller than normal. A single cause is responsible for all these manifestations: the heart is so encased by unyielding fibrous or calcified tissue as to be unable to dilate and fill properly during diastole. In some cases there is, in addition, marked constriction of the inferior vena cava. The immediate mechanisms of oedema formation are those discussed under congestive heart failure.

The milder diuretics are of little or no value in this condition, although they may occasionally lengthen the interval between abdominal paracenteses. The mercurials, however, may prove extremely useful, as in the case reported by Noth: A man aged 53 in seven and one-half years had had forty abdominal paracenteses and 450 injections of mercurial diuretics and had taken 6 gm. (90 grains) of ammonium nitrate a day for three years. At the end of this time he presented no signs of hepatic or renal injury and had been able to continue an active life as a banker. However, if the diagnosis is reasonably certain and the patient is a good operative risk, the best treatment is surgical resection of the constricting pericardium. This often results in rapid and spectacular improvement and in restoration of the patient to normal activity, even after years of invalidism.

#### NEPHRITIS

The oedema of acute nephritis is generally believed to be due in large part to widespread injury to the capillaries, which makes them more permeable than normally. It is theoretically unwise to administer diuretic drugs which might irritate an organ already acutely inflamed, and experience has shown conclusively that they are practically always devoid of beneficial action. In most cases diuretics are clearly unnecessary; if special circumstances seem to make a trial of such drugs essential, only the very mildest, such as urea or theobromine with sodium salicylate, should be used.

In chronic nephritis also diuretics are usually unnecessary if one excludes the 'nephrotic syndrome' of chronic glomerulonephritis. But if oedema becomes a serious problem almost any of the diuretics previously discussed may be used safely. The xanthines, urea and potassium salts may prove ineffective. The mercurial diuretics, combined with ammonium chloride or nitrate, are usually very satisfactory and almost never increase the renal disease. It is unwise to use these if there is acute renal inflammation or much retention of nitrogen in the blood, but extensive oedema and nitrogen retention are seldom associated.

#### HEPATIC CIRRHOSIS

It is not often that ascites and oedema of the lower extremities resulting from portal cirrhosis of the liver can be removed satisfactorily by means of diuretic drugs. It has been the almost universal experience that the milder ones, including the xanthines, urea and bismuth, are almost devoid of beneficial action. In occasional cases the mercurials, preceded by acid-forming salts, prove to be fairly satisfactory, but in most instances all that can be expected is a prolongation of the interval between abdominal paracenteses. This, however, is distinctly worth achieving, and a trial is always justified.

#### COMMENT

Even from the foregoing survey it is clear that the occurrence and removal of dropsy may present involved and baffling problems to the physician. Proper treatment of the underlying disease may result in disappearance of the oedema, but often this must be supplemented by control of the diet, by diuretics and in some cases by surgical operation. It is highly encouraging to realize that all the specific measures discussed in this article, with the exception of the xanthines, have come into general use in this country within the past fifteen years. Our knowledge of the mechanisms involved in the formation of oedema and the occurrence of diuresis have steadily widened, and our use of specific remedies has consequently become more intelligent. It is not often that the disease responsible for dropsy can be wholly cured, as in vitamin deficiency and constrictive pericarditis, but the dropsy itself can often be controlled very satisfactorily by means of medical treatment for many months or years.

### Modern Therapeutics

#### The Use and Abuse of Aperients

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It is proposed to begin with a few paragraphs on the misuse of aperients, putting forward some maxims and cautions which represent the teaching and practice of a large number of teachers of medicine and surgery.

#### SOME CAUTIONS AND MAXIMS

(1) It is unnecessary to begin the treatment of an acute fever, for example pneumonia or scarlatina, by administering an aperient.

(2) It is unnecessary, and probably harmful, to administer aperients during the course of a long febrile

illness. The constipation that accompanies such illnesses is harmless and, when the illness is over, a week or so later, no difficulty is found in getting the bowels to move again.

(3) No one has ever shown that a 'brisk purge' has any good effect in acute tonsillitis or any other acute inflammatory process.

(4) An initial purge is often recommended in the treatment of acute congestive heart failure, but experience has shown that it can be omitted. If it is not necessary, then it is merciful to refrain from giving it to a dyspnoic patient.

(5) The popular belief that a sick or sulky child should be 'dosed' is stupid and a little dangerous. The claim is made that the child is often a great deal better after the aperient, but this is beside the point, for the sulks and minor illnesses of childhood are usually evanescent. The danger of these nursery doses lies in the possibility that the child's indisposition may be due to an abdominal pain about which he does not complain, as bitter experience has taught him that a complaint of a 'tummy-ache' usually brings a dose.

(6) There is little need to emphasize the almost criminal folly of giving aperients to patients with undiagnosed abdominal pain or vomiting. It would be well if all medical students and nurses could be taught that aperients should be given only to those who are in good health, and never in the expectation that they will set right some malady or ailment.

(7) The pre-operative purge of former days has been abandoned in most surgical units. The routine post-operative purge given three or four days after an abdominal operation has also been abandoned by many surgeons (it is especially dangerous after gastro-enterostomies), but unfortunately they do not always succeed in controlling the meddlesome activity of their nursing staff; for, strange though it may seem, there are still clinics in existence in which ward sisters are allowed to prescribe aperients.

#### EFFECTS COMMON TO ALL APERIENTS

The classical division of aperients is into—*Laxatives*, which increase the bulk of the stools but do not alter their consistency; *purgatives*, which produce unformed motions; *hydragogues*, which are followed by watery stools; *drastic purgatives*, which excite an inflammatory reaction in the intestine. This is not a bad classification, but it should be remembered that it is a classification based on the intensity of the effect produced by the drug, which depends not merely on the choice of the aperient, but also on the dose given and the contents of the patient's colon.

*Consistency of the motion*.—Any aperient tends to produce a stool which is more watery than normal, for by shortening the time taken for the journey through the intestine it reduces the time available for the absorption of water in the colon.

*Gripping* is the sensation of pain produced by over-vigorous muscular action in the intestine. Those vegetable irritants (aloes, cascara, rhubarb, senna, colocynth, podophyllum and jalap), which act largely by direct stimulation of smooth muscle fibres, tend to gripe more severely than the aperients which increase peristaltic activity indirectly by increasing the bulk of the intestinal contents. But the latter too may gripe unpleasantly, especially if some resistance is offered to the passage of the fluid intestinal contents by an already formed faecal mass in the lower part of the large intestine.

*The time of action* depends to some extent on the contents of the intestine and the bodily exertions of the patient during the few hours after taking the aperient. The salines and castor oil act quickly, within a few hours, or sometimes within an hour; the vegetable aperients, as will be seen, are considerably slower.

#### THE CHIEF APERIENTS

The most useful classification of aperients is that which is based upon their mode of action.

(1) Aperients which increase the non-absorbable bulk of the intestinal contents, and thus indirectly excite increased peristaltic activity.

(2) Aperients which directly excite increased peristaltic activity by means of an irritative action on the intestinal wall.

#### (1) Increase bulk of contents

*Food and drink*.—The hearty eater and drinker is rarely constipated. If the lesson taught by this fact is borne in mind no attention need be paid to 'special diets for constipation', which tend to divert the patient's (and the practitioner's) attention from the important fact that quantity matters more than quality.

*The dried seaweeds*.—The most popular is agar-agar, which is sold under a number of trade-names. If swallowed dry it imbibes water like a sponge, but if already mixed with a liquid (as in some proprietary preparations) it cannot of course do so. Such dried seaweeds are satisfactory mild laxatives, and there is no objection to their use.

*Liquid paraffin*.—When the oil is taken already emulsified (as in many proprietary preparations) the stools become slightly softer and more bulky on account of their admixture with the emulsified oil. When the oil is taken neat it still exerts a mild aperient effect, though the exact mode of action is uncertain. It probably acts partly by virtue of its own mass and partly by interfering with the absorption of foodstuffs.

*The salines*.—Magnesium and sodium sulphate, potassium sodium tartrate and basic sodium phosphate are the salines most used, but it should be remembered that all the salts of magnesium exert an aperient action. The salines should be taken in watery solution on an empty stomach, for example on rising from bed, and the solution should be either hypotonic or isotonic; hypertonic solutions tend to excite pylorospasm, with the result that the draught leaves the stomach slowly and vomiting may occur.

The salines owe their action to the fact that the salts themselves are so poorly absorbed by the intestinal epithelium; absorption of their water of solution cannot take place past the point at which further absorption would leave in the intestine a solution of higher osmotic pressure than that of the solutes in the tissue of the intestinal wall. A 6.5 per cent solution of magnesium sulphate is isotonic with human tissue-fluids and so, if a draught containing two teaspoonfuls of magnesium sulphate is drunk, about four ounces of water will remain unabsorbed in the intestine to maintain the isotonicity of the magnesium sulphate solution. This unabsorbed water excites peristaltic waves which are transmitted to the colon, and thus the contents of the colon too are hurried on even before the saline draught has reached the caecum. A large fluid motion is passed, the volume of which is far greater than that of the original saline draught.

It should be noted that the aperient action of a saline amounts to this, that a certain volume of water is rendered non-absorbable by the intestinal epithelium. There is no evidence that magnesium sulphate exercises any direct action on the wall of the intestine, and it has been shown that little or no absorption of the salt occurs. It is interesting to note that when magnesium sulphate is injected directly into the circulation its effect is to produce narcosis, and in fact it has been employed for this purpose. It is a dangerous narcotic. The popular belief that the regular daily dose of a saline purgative is in some way deleterious is, of course, wrong. A daily dose of salts is an excellent way of securing a daily motion for patients who wish to aid Nature.

*The sulphates and sulphonamides*.—The notion that sulphates should not be given to patients who are being treated with drugs belonging to the sulphonamide group is almost certainly incorrect and has just as little theoretical or experimental support as the *ipse dixit* that eggs too are incompatible with drugs of this group.

*The irritants*.—The drugs so classed are reagents which, when brought into contact with an isolated strip

of intestine, excite muscular contractions. It is uncertain to what extent these irritants act directly on the smooth muscle and to what extent through reflexes evoked by stimulation of the epithelium or local nerve plexuses, for it is difficult to conduct decisive experiments to distinguish these modes of action. Senna has been shown to act directly on the isolated muscle-fibre, and probably other similar vegetable preparations do so too.

**The anthracene group.**—The chief members of the group are aloe, cascara, rhubarb, and senna. These act by virtue of several anthracene derivatives which they contain, and which are so slowly set free from their combination in larger molecules during the passage of the drug through the intestine that the irritant action of the anthracene derivative is not exerted until the colon has been reached. Thus the action of this group is a delayed action, and the members of the group are particularly suitable for use in 'dinner pills' to be taken after the evening meal in expectation of a result in the morning. In fact this group of drugs could not be used with safety if their active principles were liberated high in the small intestine, for then these would be freely absorbed into the blood stream, and unpleasant and possibly dangerous toxic effects would be produced.

**Pregnancy and the anthracene group.**—Violent purgation is probably always dangerous to some degree for the pregnant woman, but tradition has attached a special odium to the anthracene purgatives, and in particular to aloe. It is true that aloin (the active principle of aloe) when injected intravenously into laboratory animals causes violent contractions of the uterus, but it is most unlikely that the oral administration of an ordinary purgative dose can have any such effect in man.

**Castor oil** is non-irritating until it has undergone lipolytic digestion in the small intestine. Being a compound of glycerol and a fatty acid (ricinoleic acid) it undergoes emulsification with bile salts and digestion with lipase just as butter does, and the ricinoleic acid thus set free is an irritant, as so many other fatty acids are (compare the laxative effect of 'rich' dinner). Castor oil acts in a few hours, and rarely if ever produces any tendency to subsequent diarrhoea, probably because the ricinoleic acid is absorbed into the circulation. The constipating after-effect attributed to castor oil is probably due to nothing more recondite than the thoroughness of the evacuation which it brings about. Castor oil is an excellent aperient with no disadvantages except that it is unpalatable; it may excite vomiting even in those who find no difficulty in swallowing it, and is so thorough in its action that when misused (for example when administered to patients suffering from an acute appendicitis) it may do much harm.

**The drastic purgatives.**—These are vegetable products which contain reagents capable of not merely stimulating the wall of the intestine but of exciting an acute enteritis with a diarrhoea lasting for several days. The chief members of the group are colocynth, jalap, and podophyllum, the active principles of which are glucosides split off from resins in the course of digestion.

**Croton oil**, which contains a highly irritating resin, has been removed from the British Pharmacopœia, but it is still used in mental hospitals, as it has the merit of being tasteless when well mixed with food or drink. Among medical students it is the weapon chosen by the avenger who wishes to lay a trap for pilferers of his food supplies; the enteritis produced by a large dose may be severe enough to incapacitate the thief for several days.

**The mercury compounds.**—I never prescribe mercurial purgatives (calomel and mercury itself), and I am far from being alone in my dislike for them. The objection to their use is that in some cases even a small dose may have an unpleasantly powerful and prolonged effect, and in other cases a large dose may be required to produce even a mild laxative action. The assertion that calomel is 'chologogic' and 'antiseptic' is based solely on tradition and not on fact.

**Phenolphthalein.**—This drug has the advantage of being tasteless, and has for that reason been recommended as suitable for children if given in the form of medicated sweets; it is also an ingredient in several proprietary preparations of emulsified paraffin and a number of proprietary pills. There are two objections to its use: First, it may produce an ugly, blotchy red rash and, secondly, it is easily absorbed and excreted again in the bile (compare the use of the iodine compound in radiography), with the result that its purgative action may be repeated for several days. The mode of action of phenolphthalein is similar to that of the anthracene group in that it is a direct irritant of the wall of the intestine.

#### STRYCHNINE IN PURGATIVE PILLS

**Strychnine** has no aperient action whatsoever, and yet this poison is to be found in many proprietary pills and in at least three B. P. C. pills. It is not widely enough known that little children have been killed by swallowing a fistful of such pills in mistake for sweets; one American writer on therapeutics goes so far as to assert that it is the commonest mode of accidental strychnine poisoning. It is to be hoped that drug manufacturers will stop the reprehensibly ignorant practice of dispensing such a useless and dangerous poison as strychnine in conjunction with harmless vegetable aperients, and that all doctors will do their best to prevent the occurrence of tragedies by ceasing to prescribe pills which contain even a trace of this convulsant.

#### THE ENEMA

The ordinary soap and water enema is not always absolutely safe and harmless, though as a general rule it is so. When the large intestine is ulcerated and its wall thinned, an enema may be just as dangerous as a purgative in appendicitis, and indeed in any case of suspected disease of the lower bowel the enema is a therapeutic measure which should be employed with the greatest caution.

**Ulcerative colitis** is a comparatively rare disease, and so practitioners who find themselves called upon to treat a patient suffering from it naturally turn to their textbooks for help. Among the treatments mentioned in textbooks is to be found regular washing-out of the colon, but many physicians, of whom I am one, have formed the opinion that these wash-outs are useless, add to the patient's discomfort, and probably are harmful.

#### RECTAL CONSTIPATION

**Rectal constipation**, that is to say constipation in which the faecal mass reaches the rectum but is not passed through the anus, is not uncommon. The chief causes are muscular weakness and insensitiveness acquired through habit. A method of dealing with the trouble which sometimes succeeds in not merely relieving the patient temporarily, but in preventing recurrence, is the daily injection of glycerin, at first about one ounce, but less and less every day; after a short while some patients are cured or greatly improved. Digital breaking up of a rectal impaction is occasionally necessary in the old. There is no other way of dealing with a troublesome 'lodgment', and the hardened mass which obstructs the anus by acting as a ball-valve is usually surprisingly small. Enemas and aperients are worse than useless in this condition.

#### THE TREATMENT OF CONSTIPATION

(1) In *acute constipation*, that is to say in constipation of recent origin, aperients should be withheld until the physician feels absolutely certain that they will not do harm. No patient ever died for want of an aperient.

(2) In *chronic constipation* it is wise to assume that the patient who makes this his chief complaint has either got something more than mere constipation the matter with him, or else has some reason for visiting the practitioner other than the wish to have an aperient prescribed. Many patients consult a doctor about constipation because they fear that it may be a symptom of more serious trouble; many others wish

for an opinion about their heart or their blood pressure, but are too apprehensive to ask for it directly. In advising a patient found to be suffering simply from chronic constipation it is wise to begin by telling him three things:

(a) That chronic constipation does not poison the blood or lead to cancer, and is in fact a harmless inconvenience rather than a disease.

(b) That plenty of food and drink, so far from being dangerous and tending to produce obstruction, are Nature's method of ensuring regular motions.

(c) That the regular taking of aperients is harmless. The choice of the aperient and the frequency with which it is taken is a matter for the patient's own taste and convenience.

(3) Agar-agar or some similar water-imbibing substance is the best aperient for those who find its feeble action adequate. A saline draught in the morning is trustworthy and rapid. Aloes, cascara, senna pods, and rhubarb are more variable in their effect, but can be taken at night and will not act till the following morning. Castor oil is too nasty for most people, although it is trustworthy and effective; calomel is far too uncertain and, like the drastic purgatives, too liable to set up a short attack of painful diarrhoea.

## Treatment of Prostatic Inflammation

By KENNETH WALKER, O.B.E., F.R.C.S.

(From *Medical Press and Circular*, Vol. CCIII, 10th January, 1940, p. 27)

ALTHOUGH this series of articles deals only with treatment it is necessary to discuss in brief the symptomatology and pathology of prostatic conditions. Infections usually reach the prostate directly by way of the urethra, although a hæmatogenous infection sometimes occurs as a complication of parotitis, small-pox and cellulitis of the neck. Acute prostatitis may also form part of a hæmatogenous infection of the urinary tract by the bacillus coli communis.

The varieties of prostatitis are acute prostatitis, prostatic abscess and chronic prostatitis.

### ACUTE PROSTATITIS

This occurs most frequently as a complication of gonorrhoea and is particularly liable to occur when instruments have been passed or posterior irrigation has been carried out unskillfully or with antiseptics that are too strong. Other predisposing causes to the development of a prostatitis are bicycling, track racing, sexual excess and constipation. This being so, complete rest in bed, and the avoidance of all instrumentation or local treatment is the first essential in treatment.

The second most important measure is the application of heat to the inflamed tissues. In the case of a patient in his own home and without skilled help, the only method of achieving this is by means of hot baths and by the application of hot water bottles or poultices to the perineum and supra-pubic regions. If a nurse is available better results may be obtained by hot rectal irrigations, or by the insertion of a special rectal nozzle kept warm by the circulation through it of warm water. Later, when the patient can be moved, the application of a diathermy current directly to the inflamed prostate by means of rectal and supra-pubic electrodes will be found to be the most effective method of applying heat.

If rectal irrigations be employed, pain may be relieved by injecting into the rectum at the end of the irrigation a small enema made up of antipyrin (20 to 30 gr.) and tincture of opium (10 to 15 minims) in 10 ounces of warm water. If a nurse is not available relief is obtained by a morphia and belladonna suppository. Belladonna and atropine are believed by L. Harrison to reduce the likelihood of the development of an epididymitis, a common and troublesome complication to the prostatitis.

Attention to the bowels is of the utmost importance, and as a preliminary measure four grains of calomel

followed by a saline is useful. Should, however, it be decided to treat the infection by means of sulphanilamide, paraffin must be used as a means of securing a satisfactory action of the bowels.

The only other drug used with success in pre-sulphanilamide days was sandalwood oil, given either in 15 minim capsules, or as an emulsion. This was proved more useful than any other preparation in relieving the painful and frequent micturition that is usually a feature of prostatic inflammation. Nowadays, however, sulphanilamide enters so largely into the treatment of acute infections that all methods that conflict with its use must be abandoned. For the same reason the ingestion of large quantities of bland fluids (formerly a part of treatment) is no longer advisable.

Although several writers have stated that M. & B. 693 is the best form of sulphanilamide treatment in cases of gonorrhoea, I have not found that this is necessarily the case. Whatever be the sulphanilamide preparation that is selected, largish doses (4 to 6 grams) should be given for the first two to three days, and then reduced. As a rule not only does the temperature rapidly fall under this treatment, but so also do such distressing symptoms as frequency of micturition and strangury subside.

### PROSTATIC ABSCESS

Could the histology of the prostate be examined in a case of acute prostatitis small collections of pus would frequently be discovered in its parenchyma, collections that by coalescence and growth can easily become abscesses. Indeed, prostatic abscess is a fairly common sequel to an acute prostatitis.

The appearance of an abscess is marked by an increase in the temperature, pulse rate, toxicity and symptoms of the patient. The swelling of the prostate results in greater and greater difficulty of micturition, culminating in retention, and on rectal examination a soft area may often be detected in the general hardness of the swollen gland. If left to itself, in a large number of cases, the abscess will discharge itself into the urethra or rectum, with the immediate relief of all symptoms.

It is, however, a mistake to wait too long for such a happy event. Not only is there always a danger of that serious sequel to a prostatic abscess, pelvic cellulitis, but a poorly drained cavity in the prostate may be left that continues to discharge for weeks or even months after the abscess has burst.

Once a prostatic abscess has been diagnosed the correct treatment is drainage through a perineal incision. The operation is an easy one, requiring little experience in perineal surgery since the pus usually comes to meet the operator soon after he has made his incision and reached the lower border of the triangular ligament. The insertion of a blunt instrument in the direction of the posterior aspect of the prostate generally results in a gush of pus, and all that is then necessary is to widen the track according to the Hilton method, and to leave in place a drainage tube. With the patient sitting up in bed excellent drainage is obtained and convalescence rapid.

It is often possible to avoid an open operation by draining the abscess into the urethra. This can be done best under ocular control through an operating posterior urethroscope. The chief disadvantage, however, of such an operation is that it leaves a cavity in the prostate discharging into the urethra through a comparatively narrow channel. Convalescence is slow, and prolonged prostatic massage is necessary before all discharge disappears.

### CHRONIC PROSTATIS

The symptoms of a chronic infection may be divided into four categories: (1) urinary symptoms; (2) nervous symptoms; (3) sexual symptoms; (4) symptoms due to secondary infections, e.g., synovitis and arthritis, fibrositis, etc. No disease is more variable in the severity of the symptoms it produces than prostatitis, some patients being prostrated by a comparatively mild infection of their prostates whilst others are the



victims of a severe grade of trouble without complaining of any discomfort.

The main difficulty in the treatment of a chronic prostatic infection arises from the fact that the prostate is a highly composite gland and that no method of draining away inflammatory products is satisfactory except the drastic method of open incision. Reliance must therefore be placed on such make-shifts as prolonged prostatic massage and dilatation by the passage of large-sized bougies. Prostatic massage is indeed our 'sheet-anchor' in the treatment of chronic prostatic infections. The massage should be carried out at first two to three times weekly, and then weekly until a microscopic examination of the expressed prostatic fluid reveals that only five or six pus cells are visible in every field examined. Theoretically the patient cannot be regarded as cured until pus cells are altogether absent, but this is an ideal standard that can rarely be attained. It is important that the massage should be done with method and thoroughness, the massaging finger emptying every part of the prostate downwards and inwards towards the urethra.

The passage of a large bougie has a somewhat similar action to massage, since it stimulates a contraction of the muscle fibres of the prostate and an emptying of the distended acini of the glands. It is, however, a less useful method of treatment than is massage, and should not be repeated too often.

If massage is necessary for the treatment of deep-seated trouble, so also is posterior irrigation essential for the keeping down of surface infection. With a little patience the majority of patients can be taught to irrigate out their own bladders, according to the Janet method. The most useful fluids for this purpose are a one in five thousand solution of potassium permanganate or of oxycyanide of mercury.

Rectal diathermy is a useful but by no means essential adjunct to treatment. If this be used as a

preliminary to massage it will often be found that a greater quantity of infected secretion can be expressed than is otherwise possible. Diathermy is particularly useful in the case of patients who complain of nervous or of sexual symptoms. Another method of obtaining relief in nervous cases is to give a suppository containing ichthyol 3 grains, extract of belladonna  $\frac{1}{4}$  grain and iodide of potassium 5 grains.

Because sufferers from chronic prostatitis often become neurotic general tonic treatment is important. In the later stages of convalescence outdoor exercise, with the exception of horse riding and bicycling, should be encouraged. Nor is it necessary in the later stages of the trouble to forbid sexual intercourse, provided there be no risk of spreading gonococcal infection. Coitus results in a complete emptying of the prostatic glands and therefore can be regarded as acting similarly to massage. If indulged in too soon coitus may be painful, so that judgment must be exercised before it is permitted. Should any doubts concerning the bacteriology of the infection exist in the medical man's mind it should only be permitted with a rubber sheath.

The two complications most likely to arise during the treatment of a chronic prostatitis are epididymitis and the development of a sexual neurosis. Should the former arise all local treatment must be stopped until the swelling of the epididymis has subsided. Occasionally it happens that the epididymitis recurs every time that massage is resumed. In very troublesome cases of this kind vasotomy should be undertaken.

The development of a neurosis is avoided by looking after the patient's health and taking every opportunity to reassure him concerning his sexual future. Should symptoms of nerve strain develop it is better to interrupt all treatment and send the patient away for a holiday.

## Reviews

**THE PINEAL ORGAN. THE COMPARATIVE ANATOMY OF MEDIAN AND LATERAL EYES, WITH SPECIAL REFERENCE TO THE ORIGIN OF THE PINEAL BODY; AND A DESCRIPTION OF THE HUMAN PINEAL ORGAN CONSIDERED FROM THE CLINICAL AND SURGICAL STANDPOINTS.**—By R. J. Gladstone, M.D., F.R.C.S., F.R.S.E., D.P.H., and C. P. G. Wakeley, D.Sc., F.R.C.S., F.R.S.E., F.Z.S., F.A.C.S., F.R.A.C.S. Baillière, Tindall and Cox, London. Pp. xvi plus 528, with 324 illustrations. Price, 42s.

THIS interesting book is a study of the history of the pineal body and parietal sense organ from the standpoints of embryology, comparative anatomy and geology. The field covered by the book is so wide that few people could appreciate properly all the different sections, which cover the vast field of development and histogenesis of the pineal organ of vertebrates and invertebrates, the eyes of types which are intermediate between vertebrates and invertebrates, the relation of the median to the lateral eyes, the stricture of an adult organ, its function and the pathology, symptomatology, diagnosis, and the treatment of pineal tumours, including the operative technique. The manner in which the pineal body arises in man is fully described. In the concluding chapter the authors have discussed the nature and function of the pineal body of the human brain. But how this body has become associated with the development of the sexual system is still an enigma. The position of this organ as an endocrine gland is by no means secure.

This book constitutes an achievement in writing, in original observation and in scientific manner of description. It is one of the rare and comprehensive treatises in which a subject is approached from an

original point of view, is expanded and propounded and exhaustively portrayed. The authors, a surgeon and an anatomist of ability and experience, have the capacity of combining an abundant understanding of anatomy and physiology with a good sense of pathology. In addition, the symptomatology and the clinical picture are dealt with in a commonsense way and good judgment, devoid of fixed opinion, flexible and open-minded, which combined with the surgical experience make an excellent presentation of the whole subject.

This is a readable volume with unusually good illustrations and extensive references from world literature. The views expressed from the biological point of view are remarkably balanced, and controlled judgment with regard to the treatment of pineal affections makes the volume one of interest and of great value. The book is produced and printed in a manner befitting such an outstanding work, in a subject where so little real research has been undertaken hitherto.

R. N. C.

**THE MEDICAL ANNUAL: A YEAR BOOK OF TREATMENT AND PRACTITIONER'S INDEX.**—Edited by H. Lethby Tidy, M.A., M.D. (Oxon.), F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S. Fifty-eighth Year 1940. John Wright and Sons, Limited, Bristol (Stonebridge House). Pp. xiviii plus 604. Illustrated. Price, 20s.

In a changing world there are a few things that remain unchanged; of these the *Medical Annual* is one. It is still about the best investment for the medical practitioner and to the specialist it is invaluable, for it provides him with a rapid means of keeping up to date in collateral specialties. To the reviewer, however, it provides a problem, for there is so little scope for

general comment that is not mere repetition and so much scope for detailed review that he does not know where to begin. It is the policy of the publication, and an excellent one, to choose certain important subjects, on which there have been considerable advances in recent years, for a short but fairly complete summary of our present knowledge; this is well exemplified in the summary on hæmorrhagic diseases. This practice makes the *Medical Annual* a valuable book of reference for many years. The article referred to is by Drs. Stanley Davidson and H. W. Fullerton; it is an excellent summary of recent work and gives a very good idea of the present position, especially of the treatment of these troublesome conditions. Some light has been thrown on the pathogenesis of thrombocytopenic purpura by the observation that spleens from patients suffering from this condition contains a substance which depresses platelet formation in normal animals to a far greater extent than the same extract from normal or other diseased spleens. A very similar effect is produced by the injection of allyl-isopropyl-acetyl-carbamide (sedormid), a sedative medicament, and clinically many cases of severe purpura have followed its continued use, or even brief use in persons with a hæmorrhagic tendency. Good permanent results are claimed for splenectomy in thrombocytopenic purpura.

Our knowledge regarding prothrombin and vitamin K is advancing rapidly. What appears to be chemically-pure vitamin K has been prepared and the synthetic preparation is only a matter of time, if it has not been prepared already. The parenteral administration of vitamin K in all forms of jaundice where there is any hæmorrhagic tendency seems to be indicated, as bile appears to be necessary for its absorption from the intestinal tract.

There is a good discussion on the antacid drugs for administration in hyperchlorhydria. They are a difficult problem as most of them stimulate an increased acid secretion after they have left the stomach, and are also liable to give rise to an alkalosis. Colloidal aluminum hydroxide appears to be the most useful with magnesium trisilicate as an alternative, not yet fully tried.

There are some interesting figures showing the effect of severe hæmorrhage from a peptic ulcer on the blood. The immediate result is a loss of total blood volume—a blood count at this stage would not show any anæmia as the proportions are not disturbed; then within a few hours the blood plasma recovers its normal level—at this stage a blood count would show a marked anæmia; finally, after a matter of weeks the red cells are replaced and the blood picture is again normal. This emphasizes the importance of blood volume estimations, which are so seldom carried out in clinical practice.

We feel that we must add a mild criticism. The *Medical Annual* is essentially a practical publication and however interesting the subject may be to a small section of readers, we do not feel that it is justifiable to occupy over a page on a review of one paper on the blood groups of African natives; the review itself contains many irrelevancies. Nor on the opposite page is there much value to the practitioner in a diagram and an admittedly very short description of transfusion into the abdominal aorta, however thrilled the young surgeon may be by such a display of questionable surgical acrobatics.

The illustrations are, as usual, useful and of a high standard. This remark applies particularly to the coloured plates showing gastroscopic views of the intestinal mucosa in various conditions, taken from an article in the *British Journal of Surgery* by J. Howell Hughes. There is a very significant picture of the mucosa in early carcinoma, before there is any ulceration and therefore almost certainly no symptoms.

**PHYSIOLOGICAL CHEMISTRY: A TEXTBOOK FOR STUDENTS.**—By Albert P. Mathews, Ph.D. Sixth Edition. 1939. Baillière, Tindall and Cox, London. Pp. xvi plus 1488. Illustrated. Price, 44s.

WITHOUT doubt biochemistry plays a very important part in the practice of medicine, especially in helping

the diagnosis, prognosis and treatment. One would not be far wrong in saying that recent advances in biochemistry have gradually been transforming medicine into a perfect science and rapidly replacing the art of guessing and empiricism in the diagnosis and treatment of disease.

The present edition serves to show that the author had to work hard in bringing the rapidly changing subject into line with the modern advances so as to make it as much up-to-date as possible. This has necessitated a thorough revision of almost all the chapters of the book. The labour of the author in accomplishing this heavy task appears to have been highly successful. The book has been written in a clear, lucid and simple style and gives much valuable information to the general practitioner and senior medical student, so that they can understand many of the intricate physiological problems, not only in connection with the metabolism of the body but also in connection with other problems such as digestion, nutrition and growth, energy transformation, endocrinology, etc., in the light of clinical medicine.

We are of opinion that the book is a valuable contribution to our up to date knowledge of the physiological principles in medical practice and should prove to be useful to those for whom it is intended.

J. P. B.

**TOMOGRAPHY.**—By J. B. McDougall, M.D. (Glas.), F.R.C.P. (Ed.), F.R.S.E. 1940. H. K. Lewis and Co., Ltd., London. Pp. 73, with 110 illustrations. Price, 21s.

TOMOGRAPHY, which is best defined as sectional radiography, is the latest addition to radiological science. It provides us with a means whereby we can obtain diagnostic pictures of a previously selected section of a thick part of the body such as the chest. It is of course applicable to other parts as well; but, it is in chest radiology that the method is of particular use.

In his introduction the author points out that one of the main sources of difficulty in interpreting an ordinary skiagram of the chest is the superimposition of the shadows of the bony framework and blood vessels, bronchioles and alveoli. It is not generally appreciated, for instance, that the ribs cover two-thirds of the pulmonary fields. In the pathological chest pulmonary fibrosis, displacement of the mediastinum, pleural thickening and distorted rib shadows further increase the difficulty of interpretation.

At one time it was thought that stereoscopy would solve our problems in this respect; but for various reasons, more especially the personal factor, this method has never been widely adopted.

Following this general discussion the geometrical principles underlying the method are discussed and the technique of examination described. These call for no special remarks.

The rest of the book is occupied by a collection of tomograms with accompanying notes.

The volume as it stands gives a clear and concise account of a method of diagnosis which must in time become indispensable to every department dealing with diagnosis of pulmonary tuberculosis. The author and the publishers are to be congratulated for the mode of presentation of this new departure in diagnostic medicine.

J. A. S.

**REASSURANCE AND RELAXATION: A SHORT TEXTBOOK OF PRACTICAL PSYCHO-THERAPY DESCRIBING THE NATURE OF ANXIETY AND HOW TO INDUCE RELAXATION IN THE NERVOUS PATIENT.**—By T. S. Rippon, M.R.C.S., L.R.C.P., and P. Fletcher. George Routledge and Sons Limited, London (Broadway House, 68-74, Carter Lane, E.C.4). Pp. 221. Price, 6s.

THIS is a brief outline in simple language of what may be described as the elements of psycho-analysis.

It is clearly written and avoids the numerous technical terms that have grown up around the science of psycho-analysis so that it is readily comprehensible to



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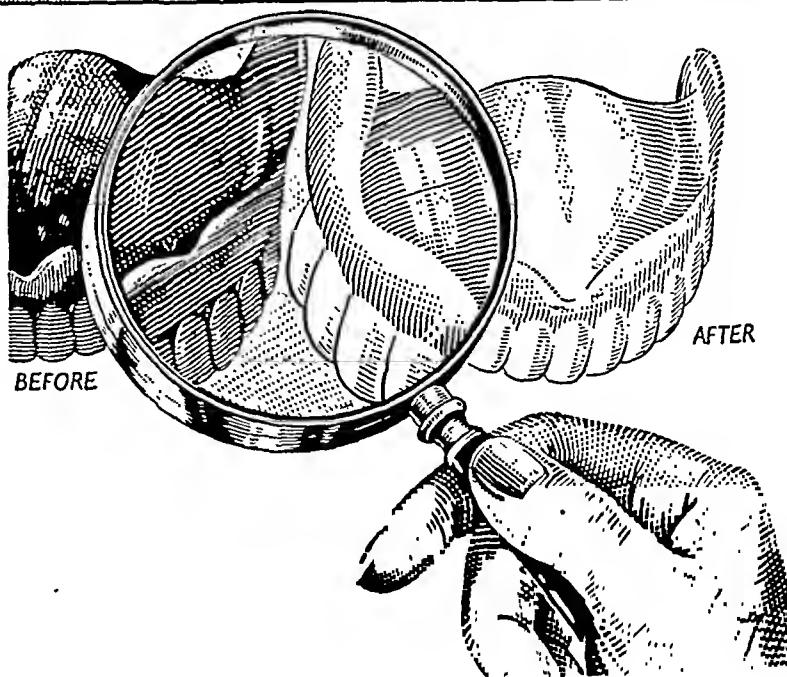
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the physician who has not studied this subject. It should be of great value to general practitioners as it gives him quite enough information as to how he can apply this aid to healing in those of his patients whose physical disability is aggravated by the simpler types of psychic trauma.

The book is also of use in indicating to the physician himself minor shortcomings that may be present in his own psychological make-up, the understanding of which cannot fail to make him a better doctor.

**PSYCHOLOGY AND PSYCHOTHERAPY.**—By William Brown, D.M. (Oxon.), D.Sc. (Lond.), F.R.C.P. Fourth Edition. 1940. Edward Arnold and Company, London. Pp. viii plus 260. Price, 12s. 6d.

ALTHOUGH the title of this book indicates its concern with the treatment of mental disorder, it actually deals with only a few aspects of treatment. Occupational therapy, hydrotherapy and 'shock' therapy, to mention a few well-established forms of mental therapy, are not even mentioned. On the other hand, psychoanalysis, hypnosis and so on are discussed at some length. The psychoanalytical psychology of Freud comes in for a good deal of adverse criticism, but the author overlooks entirely the one great flaw in psychoanalysis, *i.e.*, its disinclination to bring its principles into relation with the mental activities of non-human animals. The author appears to entertain the view that man is capable of attaining to almost any degree of sublimation, in spite of the existence of an immensity of proof against any such presumption. His optimism in respect of the results of the treatment of alcoholism and drug addiction will doubtless shock many workers in the same field, particularly in view of the crudity of the procedure which he advocates. Dr. Brown has a good deal to say on the psychology of peace and war, but omits any reference to the most penetrating study that exists on the subject in the English language, namely, 'Instincts of the Herd in Peace and War' by W. Trotter. In his chapter on 'Relation of Mind to Brain', the author shows himself to be under the spell of the fascinating philosophy of Bergson and so oblivious to the damaging criticisms to which its difficulties lay it open. The book is supplied with a copious bibliography and a tolerably good index.

O. B.-H.

**THE HISTAMINE AND INSULIN TREATMENT OF SCHIZOPHRENIA AND OTHER MENTAL DISEASES.**—By Horace Hill, M.R.C.P. 1940. Baillière, Tindall and Cox, London. Pp. vii plus 133. Price, 6s.

THIS is a very informative little book on the subject with which it deals. The writer points out that histamine is present in the body in any and every variety of shock and that a lot of the poisonous symptoms seen during shock therapy can be shown to be a mixture of the symptoms produced by poisonous doses of insulin and histamine. This induced the author to employ non-toxic doses of insulin and histamine. By this method the patient gets small repeated shocks and no 'fit'. This form of treatment is particularly favourable in its action on cases of long-standing. According to the author it is important to remember that histamine acts differently in different circumstances but always the same way under the same circumstances. As the dose suitable to each case varies so much, the author recommends keeping small quantities of the fluid of various strengths to be injected. The standard dose is 0.5 mgm. The indications for the correct dosage are the sensations of the patient and the extent and duration of the flush to which histamine gives rise, along with the pulse and respiration rates. The author recommends using three phials each containing one fluid ounce of mixtures of insulin and histamine. The amount of insulin used is 5 units while the amounts of histamine are 0.5 mgm., 1 mgm., and 1.5 mgm. Each dose is 5 minims. When the appropriate dose is found, it may be given daily for a week and then on alternate days. The author gives a number of case histories

in illustration of the type of cases treated and the results obtained.

O. B.-H.

**MY LIFE.**—By Havelock Ellis. 1940. William Holman, Limited, London. Pp. xviii plus 542. Price, 15s.

IN the preface to this book the author states that he began to write his biography as far back as 1899 and that he chose his 'Finest moments' in which to write it. The son of a sea captain, Havelock Ellis always entertained a strong liking for the sea and the ships upon it. When seven years old he went round the world in his father's ship and at the age of sixteen he went to Australia, once more on board his father's ship. In Australia he spent four happy years mostly as a school master and during a part of this period in a very lonely place called Sparkes Creek in New South Wales. Here he read and pondered over life as he saw it. He read enormously from early boyhood and throughout his life. He acquired a considerable knowledge of French literature and published in 1935 a study of French literature under the title *From Rousseau to Proust*. On his return to England he decided to become a doctor and joined St. Thomas' Hospital in London. In spite of his great intellectual gifts he had great difficulty in passing his examinations to qualify, so that it was not until seven years had passed that he took the Licentiate in Medicine, Surgery and Midwifery of the Society of Apothecaries. During the whole of the period of his medical education Ellis was deeply engaged in various forms of literary work. It was about this time that he became acquainted with the works of James Hinton whose doctrines made a profound impression on Ellis. In 1883 he made the acquaintance with the woman who played an immense part in his life, Olive Schreiner, the talented authoress of that remarkable novel, *The Story of an African Farm*. Ellis and Olive Schreiner became very devoted to each other and their friendship lasted long after each of them married. In 1891 Ellis married Edith Lees, a brilliant woman with much talent for public speaking and writing. Although sexually an invert, she did nevertheless make Ellis a devoted wife until her mental balance broke down never completely to be re-established. In 1898 the famous Bedborough trial was held in the London Central Criminal Court. The trial arose through a man named George Bedborough selling a copy of the first volume of Ellis' *Psychology of Sex* which dealt with sexual inversion. Bedborough pleaded guilty and after a long and wearisome trial was bound over in the sum of £100 to come up for judgment, when called upon. The proceedings were a reflection on the law of England and to some extent on the medical profession of England for no eminent English doctor had the courage to come forward and attest in court as to the scientific value of Ellis' book. *The Psychology of Sex* was doubtless Ellis' *magnum opus* but his exquisite prose is not to be found therein but in later works, notably *The Dance of Life*. Though afflicted at times with much sorrow and anxiety, Ellis testifies to much happiness in his life which ended in 1939. A few months before there died another great exponent of sexual psychology, Sigmund Freud.

O. B.-H.

**A TEXTBOOK OF MEDICAL JURISPRUDENCE AND TOXICOLOGY.**—By Rai Bahadur Jaising P. Modi, L.R.C.P. & S. (Edin.), L.R.F.P.S. (Glas.). Sixth Edition. 1940. Butterworth and Company (India), Limited, Incorporated in England, Phoenix Building, Graham Road, Ballard Estate, Bombay. Pp. 820 plus clv, with 3 plates (2 coloured) and 158 illustrations in the text. Price, Rs. 15

THIS excellent book by one of the pioneers in the field of forensic medicine in India has been thoroughly revised. All points referred to in the review in this paper on the last edition have received attention.

In the description of the picture of blood groups a and b should be a and b. In the technique of grouping

blood a 2 per cent suspension of red blood cells is preferable to a 5 per cent suspension.

With the advice to the practitioner to call in a consultant 'to save his own skin', when looking after a case on whom an illegal operation to procure abortion has been performed by someone else, younger medical men will not agree. An average medical man is ethically sound and his skin safe. He is not a detective. Letting an unhappy woman keep her secret is not the same thing as letting a murderer escape. Unnecessary consultation is unnecessary publicity.

War gases have been included. Gases used in household refrigeration and slimming drugs could have been included with greater justification, and so could have been manganese poisoning, a recent addition to industrial risks.

The index perhaps could be made fuller.

The paper and printing are good. No printer's errors attract attention. To the impregnated cloth used in the binding insects are rather partial.

The book should be on the desk of all medico-legal workers in India. The price is reasonable.

**TREATMENT BY DIET.**—By Clifford J. Barborka, B.S., M.S., M.D., D.Sc., F.A.C.P. Fourth Edition. Revised. 1939. J. B. Lippincott Company, Philadelphia and London. Pp. xv plus 691. Illustrated. Price, 21s.

THE book is written with the purpose of presenting to the physicians a practical and systematic method of prescribing diets and applying treatment by diet in health and disease, and also teaching the patient to make a selection of the proper amounts and types of food prescribed for him.

The first two parts deal with the subject of diet in health, the recent knowledge regarding the vitamins, their common sources, requirements, vitamin deficiency diseases, etc., and the application of diet in therapy. Part III deals with the diets in various diseased conditions, part IV, the routine hospital diets and special methods of feeding, and part V is the appendix, which contains a large amount of useful information.

In dealing with diet in each disease the author has followed a very commendable method. He has first described briefly the 'nature of the disease', the 'object of diet' and the principles that should be followed in prescribing the diet, and then the diets that are to be advised in different stages of the disease, in full detail. Most of the important diseases have been dealt with, but the serious omissions include infant feeding, diet in diarrhoeic diseases and marasmus in children.

The book is an American production, so the detailed diet tables are necessarily more suited to American and European tastes and caloric requirements. The reviewer feels that it is a pity that there is no single book in this country that contains details of dietary in health and disease, suited to the peoples of India, with diet tables consisting of indigenous foodstuffs and recipes.

The book under review will be useful to the practitioner in India in that it contains sound principles on which he can base the diet of his patients and a practical method of prescribing suitable diets, which he can modify to suit his requirements.

P. C. S. G.

**AN INTRODUCTION TO BIOCHEMISTRY.**—By W. R. Fearson, M.A., Sc.D., M.B., F.I.C. Second Edition. 1940. William Heinemann (Medical Books) Limited, London. Pp. xii plus 475. Price, 17s. 6d.

THIS is a good book on physiological chemistry which starts with a detailed account of the elements found in the living organism and then proceeds to consider the inorganic and organic compounds associated with life. The book appears to us to be admirably suitable for students entering upon higher studies in the subject. It has been written in an excellent style and the author has dealt comprehensively with the fundamental processes going on in the human body, avoiding lengthy discussions on debated points, which are often confusing to the student.

The book is up to date, well arranged and well set up. Several chapters have been entirely re-written, especially chapter II, dealing with the classification and discussion of the biological elements, the perusal of which will give a mine of information. Among other subject-matter thoroughly revised and brought up-to-date may be mentioned chapter IV, dealing with solutions and colloidal systems, chapter XII, dealing with pigments, chapter XIX, dealing with tissue respiration and chapter XXV, dealing with blood and tissue fluids.

As an admirable summary of the recent advances in biochemistry we recommend the book not only to medical students but also to all who want to be introduced to the subject of modern biochemistry.

J. P. B.

**AIDS TO PHYSICAL CHEMISTRY.**—By R. G. Austin, B.Sc. (Lond.), A.I.C., F.R.M.S. 1940. Baillière, Tindall and Cox, London. Pp. x plus 361. Illustrated. Price, 5s.

THIS handy little volume belongs to the well-known Students' Aid Series and is designed to meet the needs of students of medicine, dental and veterinary surgery, pharmacy and also of science students preparing for university intermediate examinations. Although it does not pretend to be a complete text, it has dealt with all the important aspects of physical chemistry and can be easily followed by students who have attended lectures on general theoretical chemistry. The use of mathematics has been avoided as far as possible, but the illustrative numerical examples dealing with physico-chemical measurements will assist the student in the proper understanding of the principles. Physical chemistry finds an increasing importance in the curricula of the medical students as well as in those of students of other sciences, and this volume, written in a clear and simple style by an author who has had the experience of teaching students of medicine, science and cognate subjects over many years, should prove indispensable for those who have no time to go through the larger standard texts on the subject.

S. G.

**MINERAL METABOLISM.**—By Alfred T. Shohl, M.D. 1939. Book Department, Reinhold Publishing Corporation, 330, West Forty-second Street, New York, U. S. A. Pp. x plus 384. Illustrated. Price, 30s.

THE development of knowledge in the various branches of chemical science has been so rapid during the last two or three decades that it is almost impossible for any single individual to keep in touch with all the branches outside his own speciality. To obviate this difficulty and to facilitate the work of those engaged upon different fields of chemical and physical problems, the American Chemical Society undertook, since 1919, a systematic production and publication of scientific and technical monographs on chemical subjects. The present volume is one of these publications, the main purpose of which is to describe the rôle of minerals in the structure and function of the human body.

Within the last few years, the subject of mineral metabolism has advanced by rapid strides and many eminent authorities have increased considerably the bounds of our knowledge by their valuable contributions to the subject. We welcome the present volume because it is not only a valuable addition to the list, but it has several new and interesting features of its own. In the first place it deals with the mineral composition of the body and discusses such matters as minerals of the whole body, mineral content of the different organs, etc., it then deals with the composition of the secretions and excretions and discusses the mineral composition of secretions like saliva, gastric, pancreatic and intestinal juices, bile, etc. The mineral composition of urine, faeces and sweat are then discussed. Among other subjects dealt with in the book are the mineral composition of the internal secretions of the adrenals, pituitary, parathyroid, thyroid and other glands. The chapter on the studies of the mineral intake, balance and requirements is very interesting



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and will repay perusal. We do not hesitate to recommend the book to our readers.

J. P. B.

**AIDS TO MEDICAL DIAGNOSIS.**—By Arthur J. Whiting, M.D., M.R.C.P., and G. E. Froderick Sutton, M.C., M.D., B.S. (Lond.), M.R.C.P. Fifth Edition. 1940. Baillière, Tindall and Cox, London. Pp. vii plus 293. Illustrated. Price, 5s.

This is the fifth edition of a book that is meant to help the reader in getting a good outline of the subject of medical diagnosis.

The book contains concise descriptions of the diagnostic features and differential diagnosis of the various infectious and systemic diseases. Though the subject of diagnosis of the diseases that are common in the United Kingdom has been dealt with more or less satisfactorily, there is no mention of such important diseases as malaria, kala-azar, amoebic dysentery, etc., diseases that the practitioner in the tropics has to diagnose in his day to day practice.

The fact that little attention has been paid to the tropical diseases has lessened the value of an otherwise useful book to students and practitioners in the tropics.

P. C. S. G.

**THE AUSTRALIAN ARMY MEDICAL SERVICES IN THE WAR OF 1914-1918. VOLUME II.**—By Colonel A. G. Butler, D.S.O., V.D., B.A., M.B., Ch.B. (Camb.). 1940. Australian War Memorial, Canberra. Pp. xvi plus 1010, with 212 illustrations, maps and graphs. Price, 21s.

It was a coincidence that this volume came into the hands of the reviewer on the very day that the names Peronne, Amiens, Abbeville, etc., had again begun to figure in the war news. This indicates clearly that its appearance has been too long delayed to give it any real value as a guide to field operations in the present war.

Nevertheless it is a good outline of the activities of the Australian Army Medical Corps in the second phase of its career in the Great War, that is in France and the base depôts and hospitals in England and as such it is a useful contribution to the history of the war.

Perhaps the most valuable part of the book as a guide to future Australian medical administrators is the account of the difficulties that arose at headquarters in England by the failure of the superior authority in Australia fully to appreciate the conditions in France and England, and the necessity of complying in every detail with the orders issued by the War Office. The result of this failure to understand was that the Australian medical service was often hampered by orders from Australia which were at variance with the advice sent by those on the spot in England. The same refusal to accept advice led to many men being sent as reinforcements who were unfit for the rigorous condition of service in the European winter.

If the book prevents such things occurring again in this or in subsequent wars it will have served a useful purpose.

P. A. M.

**THE PRINCIPLES OF ANATOMY: AN INTRODUCTION TO HUMAN BIOLOGY.**—By A. A. Abbie, M.D., B.S., B.Sc. (Syd.), Ph.D. (Lond.). 1940. Angus and Robertson, Limited, Sydney. Pp. 143. Illustrated. Price, 10s. 6d.

This book is stated to have been '... particularly designed to help those who come to the study of anatomy without any biological training'. Students in this category must be few and far between because even schools now give a certain amount of instruction in biology and kindred subjects, so the number of persons who take up the study of human anatomy so ill-equipped as this must be negligible.

It is little more than an illustrated dictionary of elementary anatomical terms in which the words defined are indicated throughout the text by being printed

in heavy type. It is difficult to see in what manner this book will be of any real help in the study of anatomy.

**THE ROMANCE OF TUBERCULOSIS.**—By Amiya Jiban Mookerjee. 1939. Thacker, Spink and Company (1933), Limited, Calcutta. Pp. xlv plus 196. Price, Rs. 2-8

The problem of tuberculosis, which may be truly called 'Public Enemy No. 1', is attracting the attention of the medical world and the general public, but only very few are aware of the serious nature of the disease and little is being done in this country to control its spread. In this book the author has studied and observed the problem from his life's hard experiences, thus to save others from an untimely death. The origin, growth, development, diagnosis and treatment of the disease, and the anti-tuberculosis work in India and abroad have been described well by a sufferer himself as 'the problem is no longer a monopoly of the specialists'. Those, who are interested in this country's welfare, would do well to respond to the stirring appeal made by the author by lending their greater support and help in the struggle, to combat this serious disease. Victory is assured if each one will do his part.

M. N. R. C.

**CATALOGUE OF THE GRANT MEDICAL COLLEGE LIBRARY, BOMBAY, 1939.**—Compiled by K. N. Achyut, B.A. (Bom.). Third Edition. 1940. Government Central Press, Bombay. Pp. 460. Price, Rs. 2-8 or 4s. 6d.

This is not the main catalogue of the library. The main catalogue, which is meant for the use of the readers, is maintained by means of cards and is called 'The Dictionary Card Catalogue'. The present catalogue is a printed shelf-list and is mainly intended to help the internal administration of the library such as stock taking, keeping the number of books in various classes properly balanced, preventing unnecessary duplication of copies, etc.

This shelf-list is divided into two parts. Part I contains new books which have been classified according to the Dewey System. Part II lists the old stock of books. The old accession and group numbers, as given in 1930 catalogue, are preserved in this part. This is a useful publication and will meet the requirements of those concerned.

J. N. S.

#### OTHER BOOK RECEIVED

Shell Shock in France—1914-18. Based on a War Diary kept by Charles S. Myers, C.B.E., F.R.S. 1940. The University Press, Cambridge. Pp. xi plus 146. Price, 4s. 6d.

## Abstracts from Reports

**INDIAN CHEMICAL MANUFACTURERS' ASSOCIATION: REPORT OF THE COMMITTEE FOR THE YEAR 1938-39**

The Indian Chemical Manufacturers' Association was inaugurated on the 16th July, 1938. The rapid development of the chemical and pharmaceutical industry in India has given rise to various problems and the necessity of having an all-India organization of manufacturers of chemical, pharmaceutical and allied products in India was long felt. In order, therefore, to enable the manufacturers to combine and co-operate in solving the various problems facing this industry and to put the view-point of the industry on matters concerning it before the Government and the public, the above association was started. Acharya Sir P. C. Ray, in his message at the time of inauguration, stated:

'The import of chemical, pharmaceutical and other allied products forms a substantial part of the annual drain of our wealth to foreign countries. It is a happy augury that the chemical and pharmaceutical industry is receiving adequate attention these days from entrepreneurs and many large and good factories have been established in India. With the growth of the industry, however, a number of questions are cropping up which require concerted action on behalf of all engaged in the industry. I am, therefore, glad to learn that some manufacturers are actively considering the question of establishing an Indian Chemical Manufacturers' Association and that it will be affiliated to the Indian Chamber of Commerce, which is always active in advancing the cause of the Indians. I need hardly say that the time is ripe for the formation of such an organization and I wish them every success. I trust that the association will be able to render useful service to the chemical and pharmaceutical industry.'

The Association is an organization of manufacturers of chemical, pharmaceutical and allied products and its membership is confined to manufacturers only. Besides the chemical and pharmaceutical industry, it is intended to represent the interests of manufacturers of heavy chemicals also.

The inaugural meeting, which was attended by representatives of various chemical concerns, was held at the premises of the Indian Chamber of Commerce at 135, Canning Street, Calcutta, on Saturday, the 16th July, 1938.

[The formation of this association is an important step forward in the general tendency towards the improvement in the quality of drugs which began with the Drugs Inquiry Committee in 1930 and which since that time has made slow but steady progress in many directions.—Editor, I. M. G.]

#### THE TUBERCULOSIS ASSOCIATION OF INDIA. (INCORPORATING THE KING-EMPEROR'S ANTI-TUBERCULOSIS FUND AND THE KING GEORGE THANKSGIVING (ANTI- TUBERCULOSIS) FUND): FIRST ANNUAL REPORT 1939

FOLLOWING the general approval conveyed by the the provinces and states to the draft constitution of the Tuberculosis Association of India, the Association was registered on the 23rd February under the Societies Registration Act, XXI of 1860. The King George Thanksgiving (Anti-Tuberculosis) Fund along with the King-Emperor's Anti-Tuberculosis Fund was incorporated in the new Association.

The inaugural general meeting was held at the Viceroy's House under the presidency of Her Excellency the Marchioness of Linlithgow on the 29th March, 1939. In addition to the members of the central committee the meeting was attended by the other foundation members and by two representatives from each of the major provinces, from Baluchistan and from the following states: Bhopal, Indore, Gwalior, Hyderabad, Baroda, Travancore, Mysore, Jaipur, Jodhpur and Bikaner.

At the meeting of the 30th March, 1939, the central committee of the Tuberculosis Association of India appointed Dr. C. Frimodt-Møller, C.B.E. (Hon.), M.B., Ch.B. (Copenhagen), as medical commissioner for a period of two years.

Since his appointment on 1st May, 1939, the medical commissioner has rendered help in the development of a number of tuberculosis schemes in provinces and states advising on contemplated new projects as well as on the improvement and development of existing work.

After a careful study of the tuberculosis problems in India and after personal contact with tuberculosis workers and administrators all over the country, the medical commissioner has advocated a scheme of 'Control of Tuberculosis by Organized Home Treatment' as the chief measure to aim at in the present campaign. Such a scheme requires as its foundation

a great number of modern tuberculosis clinics and a smaller number of large central tuberculosis sanatoria and tuberculosis hospitals. Without this foundation and without the establishment of close co-operation with the medical practitioners, with care and after-care committees, ex-patients' colonies, and with the government and local bodies and private organizations the scheme can never work successfully.

In his tours the medical commissioner has visited only those places whence requests have come for his visit and advice. After his visit he has drawn up a report with detailed suggestions of improvement of existing institutions and a scheme for the most effective campaign in the provinces, states or places in question. Copies of these reports have been sent to the committees and administrators concerned.

The main objectives of the Association's educational efforts are firstly to help the public towards a practical knowledge of tuberculosis, its causes and prevention, and secondly to create a public opinion favourable to the application of the necessary public health measures. By producing educative material for distribution throughout India, the centre carried on an activity which had previously been used with good effect by the King George Thanksgiving (Anti-Tuberculosis) Fund.

Propaganda material was issued free to most of the St. John Ambulance Brigade Overseas centres which organized lectures on tuberculosis in connection with their training camps. As most of the provincial and state associations came into being in the latter half of the year under review their activities in this respect naturally did not assume large proportions.

The Association maintains a large stock of pamphlets, leaflets, charts, posters, giving in plain language suitable for laymen the important facts about tuberculosis. During the year 20,584 pamphlets and leaflets, 7,925 posters and 2,050 charts were issued from the Red Cross Depot where our material is stocked.

The following new pamphlets were issued by the Association during the year:—

1. Social Service in Tuberculosis (English).
2. Planning of Tuberculosis Institutions in India (English).

During the year it has been necessary to reprint the two pamphlets:

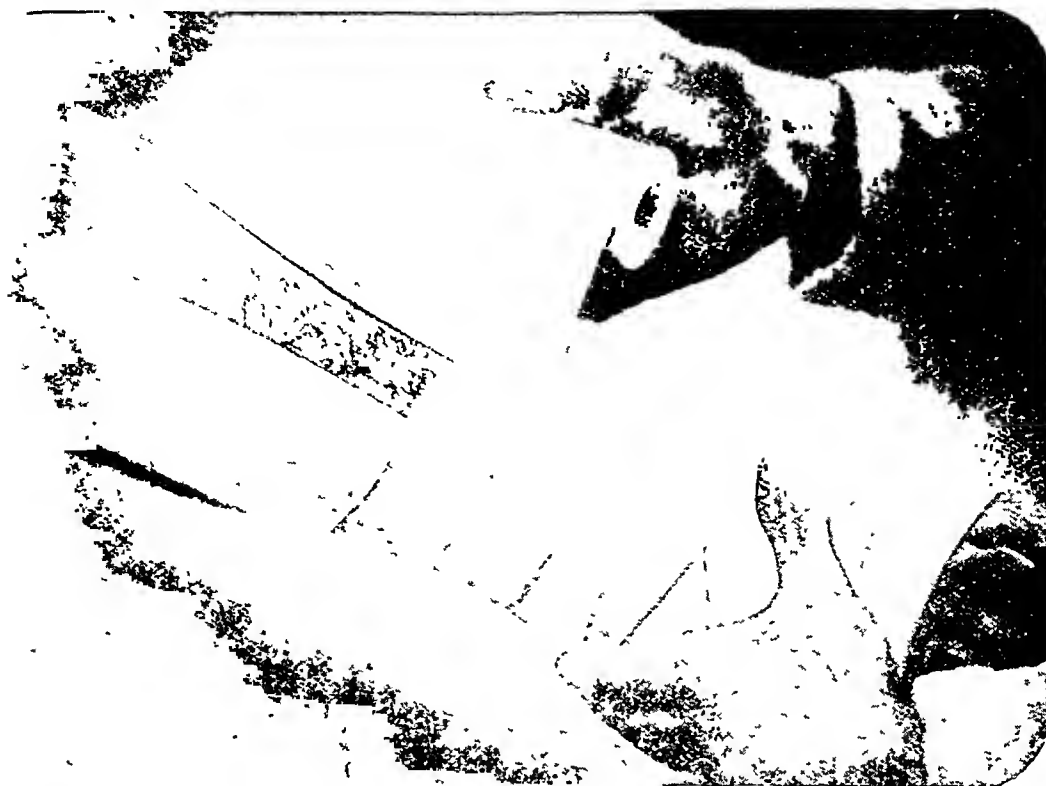
'What a Teacher should know about Tuberculosis' (English, Hindi and Urdu, 3,000 copies of each) and 'Social Service in Tuberculosis' (English, 10,000 copies).

Five sets of magic lantern slides were sold during the year and four sets lent for demonstrations by interested organizations.

Training of doctors in the preventive aspects of tuberculosis has been a successful activity under the King George Thanksgiving (Anti-Tuberculosis) Fund and this activity is therefore continued by the Tuberculosis Association of India. There has been a great demand for this training from all parts of India and during the year under review two post-graduate courses were organized, one in Calcutta (January-February 1939) and the other one in Madras (October, 1939). Fifty-five doctors selected from different provinces and states received training at these courses but the number of applicants far exceeded the accommodation available.

The short post-graduate courses are not intended for the training of tuberculosis specialists though they are of the utmost importance as a link in the chain of anti-tuberculosis measures and in fact indispensable in the present campaign.

The object of these courses is to supply doctors with the knowledge of the new developments of treatment and of the various problems of tuberculosis, so that they may be able to co-operate effectively with the tuberculosis specialists in charge of the institutions. Without such an understanding no effective co-operation will be possible between the doctors and the tuberculosis clinics, and without such a co-operation the scheme of 'Control of Tuberculosis by Organized Home Treatment' which is now being inaugurated all over India cannot achieve the results hoped for.



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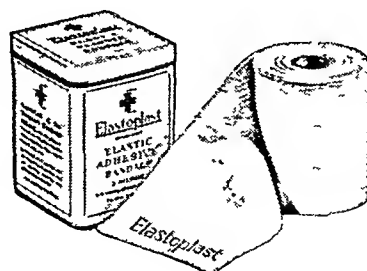
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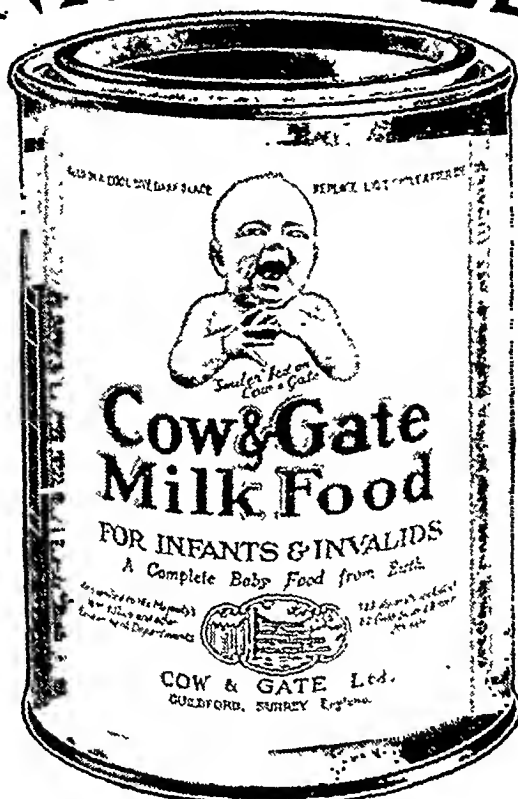
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(per 100 grammes)	481	60.0
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One of the essential parts in the campaign against tuberculosis is the provision of a sufficient number of doctors fully trained in the modern methods of diagnosis and treatment who can take charge of tuberculosis institutions. Unfortunately there are at present in the whole of India only a few places where doctors can be given the proper training. Therefore one of the first measures in the campaign in India is that each province and state should concentrate its efforts to establish a large tuberculosis training centre, before clinics are widely organized.

According to the scheme passed by the King George Thanksgiving (Anti-Tuberculosis) Fund Committee a course for the training of tuberculosis health visitors was organized at Delhi from the 16th January to 15th July, 1939. At the request of the Fund Committee the authorities of the Lady Reading Health School and the Delhi Municipality very kindly agreed to give all the facilities for the above course at their institutions.

At the termination of the course the candidates were examined in the following subjects:—

Home Nursing, Hygiene, Domestic Sciences and Tuberculosis.

Out of ten candidates, nine passed and one who failed to come up to the required standard was re-examined after a month's extra training and was declared successful.

The first conference of tuberculosis workers organized by the Tuberculosis Association of India was opened by Her Excellency the Marchioness of Linlithgow, the President of the Tuberculosis Association of India, in the Red Cross Conference Hall on the 20th November, 1939.

This is the third year in succession in which the editor of the *Indian Medical Gazette*, at the request of the Central Tuberculosis Organization, has issued a special tuberculosis number of the *Indian Medical Gazette*.

The special tuberculosis numbers have been very popular not only in this country but have attracted considerable attention outside India and the editor has received a number of appreciative letters from prominent tuberculosis workers in other countries.

A summary of tuberculosis news giving brief reviews of tuberculosis activities in India, has been contributed to the *Indian Medical Gazette* from time to time during the year.

The constitution of eleven provincial and of six state tuberculosis associations has during this year satisfied the conditions of affiliation as defined in the by-laws of the Central Associations and these associations have consequently been affiliated to the Tuberculosis Association of India.

Her Excellency the Marchioness of Linlithgow desired that a sum of Rs. 1 lac should be set aside for the construction of a Tuberculosis Model Clinic in Delhi and that when the clinic comes into existence the Tuberculosis Association of India should make a yearly contribution of Rs. 4,000 to this institution 'a controlling interest in the clinic in order that full use of it can be made for training and experimental purposes'. The central committee has resolved that steps should be taken to give effect to the conditions contained in Her Excellency's letter.

Dr. C. Frimodt-Møller visited the Pasteur Institute of India, Kasauli, in February 1939, with the object of reporting on the possibility of converting the Pasteur Institute into a sanatorium. After a study of the site and buildings he gave his opinion that if funds were available it would be possible to establish a sanatorium for 110 beds in the first instance with the possibility of development to 200 to 250 beds, with all modern facilities for treatment of pulmonary tuberculosis.

The Kasauli Sanatorium when established should be a centre for the training of doctors in tuberculosis for the whole of Northern India.

The Executive Sub-Committee of the Tuberculosis Association of India awarded the Hassan Masud Suhrawardy Memorial Anti-Tuberculosis Challenge

Shield to the Station Municipality, Bangalore, in recognition of a commendable effort made by a young organization in the anti-tuberculosis field.

Research on tuberculosis in India so far as it is undertaken at present is largely financed by the Indian Research Fund Association. The promotion of research in tuberculosis is also one of the activities of the Tuberculosis Association of India but as this Association is not at present in a position to support tuberculosis research on a large scale, it was decided to make a grant of Rs. 4,000 to the Indian Research Fund Association for expenditure during 1940 on research work in tuberculosis subject to the condition that the programme of work is approved by the Chairman of the Tuberculosis Association of India.

The Tuberculosis Association of India succeeded the King George Thanksgiving (Anti-Tuberculosis) Fund as the national representative of India on the International Union against Tuberculosis. The Association was represented on the Union by Major-General E. W. C. Bradfield and Dr. C. Frimodt-Møller as councillor members.

The year under review has been one of transition with the inauguration of new activities both in connection with existing institutions and schemes and in the planning and development of the campaign as a whole. Many new provincial and state tuberculosis associations have been formed and the affiliation of 17 to the Central Association has been completed.

#### ANNUAL REPORT OF THE INSTITUTE FOR MEDICAL RESEARCH, FEDERATED MALAY STATES, FOR THE YEAR 1938. BY A. NEAVE KINGSBURY, DIRECTOR

ENDEMIC areas of filariasis often have a considerable simian population. A number of monkeys (*Macaca irus*) have been trapped and examined. Three of ten were found to harbour microfilaria morphologically similar to *Mf. malayi*. It has been shown that these readily infect *M. longipalpis* and *M. uniformis* and that neither mature nor immature larvae could be distinguished from those of *Mf. malayi*. The experimental transmission of the latter to *Macaca irus* is in progress. The difficult problem of filariasis control will be still further complicated if the simian parasite proves also to be pathogenic to man. This is a matter of considerable public health interest which as yet remains an open question. The importance of *M. longipalpis* as the principal local vector of *Mf. malayi* has been demonstrated, though other species of *Mansonia*, if plentiful, may play a part.

The tuberculosis survey has been extended and the results of the Mantoux test on upwards of 3,000 Kuala Lumpur children are recorded. The parents of Tamil children in the local schools are largely of the 'clerical' class or artisans in the employ of Government: these children consequently enjoy good housing and reasonable dietary and it is noteworthy that the percentage of positive reactors is little more than half that for Chinese and Malay children. Among the latter there is a significant and sudden rise in the percentage of positives at about fourteen years of age; shortly before that age they pass from vernacular to 'English' schools where they mix freely with the more heavily-infected Chinese.

Apart from the Malays—few figures are available for the female children of that race—the rates for males and females are very similar, suggesting that the home is the main venue of infection. Chinese children appear to be the most heavily infected. Although this is probably due to crowded conditions of living with consequently massive infecting doses, racial susceptibility to allergy may perhaps be a factor contributing to these results. The general rates are high and indicate that unless there is considerable improvement in the general standard of living, no appreciable decrease in clinical tuberculosis can be expected within the next decade.

Experiments on the chemo-prophylaxis of malaria have been continued. Plasmoquine in an adult dosage



of 0.02 gm. twice weekly was given to the whole population (excepting very young children) of estate 'T' on which hyper-endemic malaria, mainly due to *P. vivax*, prevails. The numbers were large—five hundred rising to seven hundred—and the attendance at treatment musters averaged over ninety-five per cent. Gauged by malarial incidence, trophozoite and gametocyte rates, infection of new arrivals and of newly-born children, the effect was disappointing. Infected anophelines continued to be trapped at about the same rate as formerly, though from eighty *A. umbrosus* and *A. novumbrosus* dissected after feeding on *P. vivax* gametocyte carriers who had had plasmoquine within four days, oöcysts only have so far been obtained in two instances.

Trapping has been continued on this estate. In the first six months of the year the catches of *A. novumbrosus* were as numerous as those of *A. umbrosus*. Dry weather commenced in May, continuing until August and, as in 1937, *A. novumbrosus* did not, except for occasional specimens, reappear until November. In the case of *A. umbrosus*, however, there was no evidence of seasonal periodicity. Projected extensions to the estate have necessitated the felling of a large area of contiguous jungle, and probably as the result of this clearing, a few *A. maculatus* were taken during the year. It is of interest that this species had been unrepresented in the catches over the previous three years. The nearest hilly ground on which breeding is known to occur is five miles distant from the trap and three and a half miles from the new clearing: the intervening land is swampy and covered with high jungle.

On another estate the population was divided into three groups. Atebrin in a dosage of 0.3 gm. once weekly and of 0.3 gm. daily for five days every fifth week was given to two of the groups, while the third provided a 'control'. The regular weekly dosage was found to have considerably greater prophylactic value.

New anti-malarial remedies tested included 'Certuna', 'A. granulate', 'Malarin', 'Malario' and 'Sulphanilamide'. The last three will find little place in the therapeutics of malaria for all proved to be less effective in the treatment of malignant and benign tertian infections than quinine. 'Certuna', however, is of greater interest for Kikuth and Hecht have found its action on the gametocytes of *P. cathemerium* to be more potent than that of plasmoquine, while Sioli and Muhlen, and Missiroli have reported that it was less toxic. The virtue of 'Certuna' is claimed to reside in its gametocidal properties. Preliminary observations indicate that its value as a schizonticide in *P. vivax* and *P. falciparum* infections is small and that, as a gametocide, its value is similar to that of plasmoquine for *P. falciparum* but somewhat inferior to it for *P. vivax*. This drug may have been a causal factor in a case of mild acute bulbar paralysis. Another interesting new drug tested during the year was 'A. granulate', which has been developed to facilitate administration to children. In therapeutic value, however, the results, up to the present, point to a marked inferiority *vis-a-vis* atebrin, to which it is chemically allied.

The use of mosquito traps has been advocated for many years past and it is gratifying that the method is being more and more employed by health authorities. Among a batch of trapped anophelines forwarded for dissection from Bagan Datoh, one *A. sundanicus* was found with sporozoites in the glands. This was the first of that species to be found infected of over 4,000 dissected by the Entomological Division in the past five years.

Investigations of anti-larval oils have been continued and field experiments are now in progress. The effect of the addition of small quantities of pyrethrum has been tested: the rapidity of kill was often increased but the final mortality was unaltered for oils that are employed for anti-malarial purposes.

The study of local typhus fevers has been continued. The mutation of an X19 rat strain on transmission by *X. cheopsis* to the XK type has again been observed. As far as experiments have progressed, it appears that Sumatran mite fever and tsutsugamushi (Japanese

river fever) are probably one and the same disease; our Dutch colleagues, however, inclined to a different view.

Experiments relating to the preparation of a prophylactic vaccine against Japanese river fever has continued, though the protection of experimental animals has not yet been achieved.

The immunization of a horse against Japanese river fever has been continued with enormous quantities (1,000,000 guinea-pig infecting doses) of virus. After this last immunizing course two c.c.m. of the serum failed to protect guinea-pigs against ten infecting doses of virus. The serum was then concentrated (approximately 5/1), after which its effect had greater promise.

It is of interest that the demand for rice polishings extract has doubled in the past two years and quadrupled since 1933. Certain proprietary preparations have been assayed for vitamin-B<sub>1</sub> content and the time appears to be not far distant when synthetic products will provide an economic substitute for the rice polishings extract.

It is widely held that rice, parboiled in ordinary cooking utensils, retains considerable vitamin B<sub>1</sub>, irrespective of the degree of subsequent milling, if not subjected to excessive washing. But occasional commercial samples, probably through exposure to unduly high temperatures during parboiling, show marked vitamin loss. Extensive experiments are in progress with a view to defining conditions for controlled parboiling.

The report of the Division of Chemistry includes an interesting table showing the percentage of milk samples that have been found adulterated over the past ten years. This malpractice is far too common and continues practically unabated by the fines inflicted by magistrates.

Lymphogranuloma inguinale is being further investigated. Seventy-five suspected and control cases were tested with Frei antigen and also with an emulsion of Ducrey's bacilli. Positive results with the Frei antigen were obtained in fifteen cases of subacute inguinal bubo and in four cases of stricture of the rectum. Three cases reacted favourably under 'Sulphanilamide' treatment.

With a view to the further refinement of routine tests for the 'grouping' of blood stains, preliminary investigations with anti-'M' and 'N' sera have been made. Sera have been prepared and adsorbed. The results with experimental stains from 0.02 c.c.m. of blood proved inconclusive, but with double that quantity of blood the reactions were more definite. The number of exhibits of blood stains submitted by the police in the past year approached six hundred. On sixty-two of these 'A' and 'B' grouping was attempted with conclusive results in forty-nine instances.

For the routine diagnosis of early pregnancy two rabbits are utilized, one being injected with fifteen c.c.m. of urine, the other with a concentrate from fifty c.c.m. Tests on local rabbits have shown that hæmorrhagic ovarian follicles develop after the injection of about fifty rat units of gonadotropic hormone. The quantity of urine utilized in the routine test—if from cases of early pregnancy—should thus contain ample hormone to induce positive results. In tests on thirty-one of fifty-three specimens submitted from cases of doubtful pregnancy, hæmorrhagic follicles were seen, but in nine of these the 'concentration' method alone gave positive results. It appears that either the hormone content of the specimens was unduly low or a considerable loss had occurred during transit.

Experimental work on methods of rat destruction has been continued. The toxins of *B. dysenteriae* (Shiga), *S. enteritidis* 'Liverpool', and *Cl. botulinum* have proved relatively innocuous to local rats. The collection of biological data has been extended and the ratcidal value of certain commercial and other poison baits has been examined.

The work of the Lymph Station continued to be satisfactory. Following a fall in the vaccination success rate in one district, tubes of a batch of lymph were returned for re-testing. The rabbit potency had fallen to about one-seventh of its original value and the



# The Value of Dietary Supplements

*A Summary of Investigations\* published in the  
"Medical Officer," March 30 and April 6, 1935*

A NUMBER of children, all receiving their customary home diet, were given either No Supplement, Cod Liver Oil, Halibut Liver Oil (with milk to provide equal calories) or Virol. The experimental scheme provided that each child should have a period on each treatment in turn, in such a way that every possible sequence was included. Rigid statistical control was thus possible.

## Gain or Loss in Weight on Various Supplements :—

Supplement	Total gain in ozs. over all periods	Average gain per child per week in ozs. over all periods	Total loss in ozs. during summer period only	Average loss per child per week in ozs. during summer period only
No Supplement - -	88	0.3	— 103	— 1.4
Cod Liver Oil - -	287	1.0	— 77	— 1.1
Halibut Liver Oil with milk - - - -	333	1.2	— 184	— 2.6
VIROL - - - - -	762	2.6	— 7	— 0.1

Whereas earlier investigations had shown that the mere addition of vitamins had no effect on growth, these investigations have conclusively proved that Virol—a balanced food containing all the necessary vitamins—has a definite and remarkable effect in bringing the rate of growth up to the recommended standard. Virol was the only one of the supplements used that promoted this ideal rate of growth.

Virol was the one and only preparation that maintained the children's weight in the hot weather.

\* The full report will be sent on application to Messrs. A. H. Wheeler & Co.,  
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- (2) The nature and physical state of the proteins,

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results of infant vaccination were also indicative of deterioration. It is believed that the vaccinator had failed to return unused tubes to cold storage after the completion of his rounds. Attention is again invited to the importance of the careful supervision of conditions of lymph storage.

[The above abstract from the general review, by the Director, indicates the valuable work being carried out by this research institute. All research workers in tropical medicine should obtain a copy of this report because they are sure to find in it something of value touching their own work. This applies particularly to workers in India where our problems are closely allied to those of the Federated Malay States.—EDITOR, I. M. G.]

# ABSTRACT OF THE ANNUAL REPORT OF THE CENTRAL NARCOTICS INTELLIGENCE BUREAU, EGYPTIAN GOVERNMENT, FOR THE YEAR 1939. BY T. W. RUSSELL, LEWA

In my annual report for 1938 I stated:—

'The official figures published in this report, while not showing any big relapse to drug addiction, do bear out the need of the warning that I expressed in my 1937 report against any self-complacency as to results obtained and against any slackening off in preventive effort.

... the slightest relaxation of police effort in Egypt or the slightest enfeeblement of anti-narcotic policy will quickly see this country drifting back to where she was ten years ago'.

In reviewing the situation for 1939 I must repeat that warning but still more emphatically.

The total of traffickers in the State prisons on 1st October has increased since that date last year by 754 and that of addicts by 52, i.e., a total increase of 806 persons imprisoned under the Narcotic Law: this means that after steadily improving up to 1937 we have now slipped back on the general total to where we were in 1934.

As regards quantities of drugs seized in the contraband trade, fewer drugs have been seized than during the previous year.

If we take it that the police effort has remained constant, a reduction in drugs seized might be considered as proof of fewer drugs coming in.

Again an increased number of traffickers arrested might be taken as showing increased energy and zeal on the part of the police: it might, on the other hand, mean a large increase in traffickers of whom the usual proportion only have been arrested.

On the whole I believe that more black drugs than formerly are getting into the country, that police energy has not actually diminished, that, on the other hand, it has not increased in proportion to the increased traffic and that addiction to hashish and opium is definitely growing greater.

It can be taken as a basic fact that the only deterrent to drugs entering the country is the energy of the preventive services; the desire for drugs remains but cannot be indulged in so long as the preventive cordon is efficient. Failure on the part of the police to keep level with the increased trafficking is largely due to the increased preoccupation of the police, especially in the provinces, with the mass of crime work which they cannot escape.

Narcotic trafficking, unlike murders and robberies, does not force itself upon a provincial police officer's attention: it has to be looked for and time and patience spent in its detection. What provincial police officer to-day has the leisure for this voluntary work?

In the cities, and especially the port cities, the Bureau still has specialized narcotic officers and agents who keep a constant eye on the traffic; they, however, are faced with an arduous and often impossible task in trying to control contraband drugs after they have entered the country.

The mass production of hashish in Syria and of the smuggling of hashish and opium through Qantara,

makes our danger front as I have so often pointed out, the Eastern Mediterranean, the Suez Canal and the Gulf of Suez.

It is here that contraband in bulk should be seized before it has had time to enter the heart of the country and be dispersed throughout the provinces.

To do this, the coastguards and the Suez police must be equipped with powerful sea-going launches to deal with off-shore shipping.

Our Eastern front remains as dangerous as ever and beyond this front are the countries of origin, Syria for hashish, Turkey for opium and the Far East for white drugs.

In my speech this year at Geneva, I paid a tribute of thanks on behalf of the Egyptian Government to the French Authorities in Syria for their continued and successful efforts to prevent the illicit cultivation of hashish in the Lebanon. The shock was, therefore, considerable when I received in the month of June a long cypher cable to the effect that vast areas of hashish cultivation had again been discovered in those districts.

The task of repressing hashish cultivation in Syria has always been an arduous and invidious one for the French authorities when the geographical features of the country, the poverty of the villagers and the high profit to be made are realized. In spite of these difficulties, however, the Sirété have been able these last few years to enforce the laws prohibiting this cultivation all over Syria, except for small areas hidden away in the mountainous regions of the Lebanon.

How came it then that suddenly the situation had changed from little or no cultivation to square miles of it?

An indication of where the answer would eventually be found was given in the first telegraphic news received that on 28th June, M. Colombani himself and a force of police and military had discovered in the neighbourhood of the village of Laboué 5 hectares (50,000 square metres) of hashish cultivation and has proved that it was the property of a member of the cabinet.

This was followed on 11th July, by the seizure of 17 sacks of hashish powder, weighing 270 kilogrammes, in the house of a near relative of the same cabinet minister.

It was soon evident that many of the governing classes of the Lebanon had defied the Mandatory Authorities and planted vast areas of hashish cultivation, with the natural result that the smaller landowners had followed their example thinking that they could do so with impunity.

For weeks after these discoveries, the Syrian press indulged in a furious battle for and against hashish cultivation and for pure cynical opportunism I cannot do better than quote the 'Saout El-Ahrar' for 18th July, which wrote:—

'I do not believe that the breaking of the regulations of the League of Nations constitutes a crime when one considers the numerous infringements by the most civilized European countries of the basic Laws of the League. So far as harm to humanity goes, I do not think that one could charge with crime a feeble and poor people who, not willing to die of starvation, allow the foreigner to die by the slow and joyful method of hashish. We have been led to this conviction after having witnessed the great evils inflicted by the civilized races on more feeble races. Killing a race is of far greater importance than the export of hashish to habitual consumers who have the money to procure it elsewhere'.

So now we know what Egypt may expect if the hashish growers of the Lebanon have their own way.

It is difficult enough, as I have said, to keep out of Egypt the not inconsiderable quantities of hashish and opium that annually escape the control of our neighbouring countries. What, then, would have been the situation this year in Egypt had sixteen hundred tons of hashish been thrown against our eastern defences?

There is only one answer which is that, owing to the weight of the attack and to the weakness of our defences, several hundred tons would have got through.

Egypt owes a deep debt of gratitude to the French Government, and to M. Colombani in particular, for averting this mass attack on the enemy.

We can only hope that by next year the energy of the French Government and the preventive measures of our own Government will have been doubled and trebled.

To conclude I will sum up my opinion on the situation as I see it to-day.

*The four great dangers:*

(1) *Desire*.—The desire for narcotic drugs in Egypt is not exorcised: it remains very much alive and will continue so for as long as the present unsatisfactory economic and physical condition of the general mass of the population is permitted to persist.

(2) *War*.—It was war which brought the white drugs to Egypt. It has taken us the best part of ten years to defeat the drug effects of that war on Egypt. You may be sure that in this new war which has hardly yet begun every drug trafficker in the world is gleefully looking forward to profits on a far vaster scale.

(3) *Far East*.—Mass production of white drugs in the Far East is undoubtedly continuing unchecked and is likely to grow in volume if and when the big nations start mutual massacre on a large scale. This is where the drug traffickers will concentrate for their deadly munitions of war.

(4) *Syria and Lebanon*.—The danger last year of Egypt's being flooded with Lebanese hashish was imminent.

## ANNUAL REPORT ON THE HEALTH OF THE ARMY IN INDIA FOR THE YEAR 1938. VOLUME I. BY THE DIRECTOR OF MEDICAL SERVICES IN INDIA

A RECORD low figure for pulmonary tuberculosis for British troops over the last twelve years in the Northern Command, remarkably small admission rates among Indian troops in Waziristan and persistently low admission rates for malaria and sandfly fever, are some of the features of this report issued for the first time as a separate volume. Previously the report was issued as volume II of the Annual Report of the Public Health Commissioner with the Government of India.

Over the five-year periods since 1918 admission rates among British troops have shown a tendency to become stabilized at a figure approaching pre-war (1914-18) rates, while the rate for officers is distinctly lower. But invaliding shows no sign of reduction.

Admission rates generally rose by 36 per 1,000. Actual admissions however showed a drop of nearly 900. The principal causes of admission, with the admission rates per 1,000, were: malaria (50.4), cellulitis (45.2), tonsillitis (33.7), dysentery (26.8), and sandfly fever (24.8).

Death rates also went up slightly, but invaliding rates dropped by 1.6 per 1,000. The chief causes of death were infectious diseases and pulmonary tuberculosis, while those of invaliding were mental diseases.

The number of working days lost owing to disease was 822,195 compared with 878,997 days lost in 1937.

The incidence of malaria among British troops was higher than in 1937 but otherwise lower than any other year and was half the figure recorded in 1919. Among Indian troops the figures for 1938 were only higher than that for 1937 and half the 1933 figure. The return of troops infected in Waziristan led to an increase in relapse cases in other areas, but cases in the Western Independent District showed a big drop.

Lahore Cantonment, the dreaded Mian Mir, shows what anti-malarial measures can achieve. Cases among British troops which stood at 617.70 per 1,000 in 1924 dropped to 19.67 in 1938.

Sandfly fever among the British troops remained at the same level, reductions in admissions elsewhere being offset by an increase in the Western Independent District. Figures for the Northern Command and Landikotal, a hotbed of sandfly fever, showed a considerable fall.

The incidence of dengue fever fell considerably in 1938, both for British and Indian troops, figures in both cases being a fraction of those for 1937 and lower than those of the five preceding years given.

The incidence of enteric among both British and Indian troops was below one per 1,000. On the other hand dysentery and diarrhoea showed an increase both among British and Indian troops. The proximity of insanitary hazaar areas is one factor in the spread of these fly-borne diseases.

In spite of widespread epidemics of cholera there were only 42 cases among Indian troops, 41 of them in a Gurkha battalion on its arrival at Razani in Waziristan.

There were only 11 cases of smallpox among British troops and their families, while respiratory diseases showed a slight increase.

Admission rates among women and children have decreased over the past three years. The dysentery-diarrhoea group accounted for 21 per cent of the total admissions, tonsillitis and bronchitis together for about 16 per cent.

In the Indian Army, admissions among officers showed a continued increase, digestive diseases, local injuries and malaria being the principal causes. Among the soldiers the fall in admissions recorded over ten years continued. The rate for 1938 was 421.8 per 1,000 and the average for 1935-38 was less than the average for the five-year period 1930-34 by 37.6. The death rate showed an increase over the 1937 figure, while invaliding was practically stationary.

Tuberculosis accounted for about one-third of the invaliding. Cases of oriental sore were numerous in Quetta and a special grant was made by Government to control the infection. Admissions for heat stroke were the highest for several years.

Among followers the admission rate of 272.0 per 1,000 was lower than for any of the preceding five years. Special attention has been paid to the conditions of work of welders and painters in arsenals.

The percentage of rejections at recruiting centres rose from 35.73 in 1937 to 43.5 in 1938. The growing incidence of trachoma among promising candidates in the Delhi recruiting area has caused a considerable concern to the Indian Soldiers' Board.

A steady increase in the welfare work among the families of Indian soldiers was noted in 1938. The movement, run with grants, donations and annual allotments from public and semi-public funds, is also largely supported by officers and their wives and by the men of the regiments themselves both financially and with their services. There is a constant cry for more funds owing to the increasing demand.

Altogether during the year 84,677 women and 100,367 children were treated.

## Service Notes

### APPOINTMENTS AND TRANSFERS

COLONEL A. C. MUNRO, K.H.P., to be Officiating Deputy Director of Medical Services, Northern Command. Dated 6th May, 1940.

Colonel D. F. Murphy, M.C., V.H.S., to be Officiating Assistant Director of Medical Services, Western (Independent) District. Dated 13th May, 1940.

Colonel A. C. Macrae to be Officiating Assistant Director of Medical Services, Peshawar District. Dated 30th May, 1940.

Lieutenant-Colonel M. P. Atkinson, an Agency Surgeon, is appointed as Medical Officer in charge of the Crown Representative's Police Force Hospital, Neemuch, with effect from the forenoon of the 22nd May, 1940.

Lieutenant-Colonel S. M. A. Faruki, to be Officiating Officer Commanding, Indian Military Hospital, Rawalpindi. Dated 26th May, 1940.

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weighing the heart in the  
presence of the Ape of  
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## Notes

### CYCLONAL SODIUM

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For induction, short basal narcosis and total anaesthesia Sodium N-methyl-C-C-cyclohexenylmethylmalonylurea has been widely used during the past few years, although its manufacture has not been undertaken within the Empire. Now, however, the preparation is being produced in Great Britain by May and Baker, Ltd., under the name of Cyclonal sodium, and supplies are available for immediate delivery.

Full details of the properties, clinical applications, administration, dosage and packings of this intravenous anaesthetic are contained in 60-page 'Cyclonal sodium' booklet which has recently been sent to us. Its administration intravenously and rectally is also described together with the therapeutic applications of the drug. A copy of the booklet will, we understand, be sent to any member of the medical profession on request to: Messrs. May and Baker (India), Ltd., 11, Clive Street, Calcutta, India.

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#### THE TREATMENT OF CARDIAC DROPSY AND HYDRÆMIC NEPHRITIS

THIS preparation is of considerable value in the conditions indicated, for it possesses the active diuretic properties of mercury in a relatively non-irritant form. It is well tolerated both locally and generally, and administration may be prolonged in suitable cases for a period of many months.

We understand that a copy of the new Neptal publication, which includes full details of dosage, indications and technique of administration, will be sent free to any member of the medical profession on request to: Messrs. May and Baker (India), Ltd., 11, Clive Street, Calcutta, India.

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## Original Articles

### TAKING BLOOD FOR TRANSFUSION (IN POTAIN'S ASPIRATOR). FURTHER DETAILS INCLUDING COLD STORAGE

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and

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(Received for publication on 22nd June, 1940)

THE intention is to supplement what has been said under the titles 'Taking Blood for Transfusion' (Greval and Chandra, 1940) and 'The Needle in the Vein' (Greval, 1940). The necessity for giving further details has been made clear by private correspondence on the subject and by further work which has since been done.

#### 1. Sterilization of the special stopper of Potain's aspirator and tubes

Originally they were sterilized by boiling. Now they are autoclaved in small drums, like surgical dressings. The dryness of the tubes (rubber and metal) does not interfere with the flow of blood. Several stoppers and tubes can be sterilized together and taken out with the same precautions with which surgical dressings are taken out.

#### 2. Sterility of the blood taken for storage

The contrivance described for taking blood for transfusion was originally intended for bleeding a donor, and using the blood within an hour or so. The precautions taken aimed at surgical asepsis but not bacteriological sterility. It was, however, found that blood taken by the same device for injecting animals and kept for several weeks in the cold remained free from signs of contamination. The blood stays at room temperature for half an hour, and presumably during this period its immunological forces deal effectively with the stray micro-organismal intruders. Sterile nutrient broth bottled like the blood is not likely to stay sterile.

Incidentally, the writers now use plain sodium citrate solution instead of Rous and Turner's solution in taking and keeping human blood for producing anti-M and anti-N fluids (Greval, Chandra and Woodhead, 1939).

#### 3. The pump

The pump of Potain's aspirator is not damaged by the water vapour or even water sucked from the boiled knotted tube. The heat generated in action appears to dehumidify it. Cheap pumps costing Rs. 10 are (or have been) available. Powder from new tubes blocks the

pump. An ordinary 20 c.cm. Record syringe used with a two-way adapter can also be used in the place of the pump. The air is sucked from the bottle and discharged outside by opening and closing the necessary way. Twenty to thirty strokes suffice as is the case when the pump is used.

#### 4. Coagulation of the blood in the tube and bottle

Clotting occasionally occurs in the tube between the vein and the bottle and stops the flow of blood. This appears to be due to two causes. The first cause is the obstruction to the flow by too many joints. The writers now do not employ tubes with glass windows (the incoming tube in the original apparatus has a glass window). The second cause is the abnormally high coagulability of some bloods. The clotting occurs when about 200 c.cm. of blood have been drawn. More can be drawn from the other arm in another bottle. The unavoidable excess of sodium citrate in the first bottle, if the intended quantity was more than the quantity drawn, is an advantage and should be intentionally allowed in the second bottle, otherwise a part of such blood will coagulate in the bottle later.

Donors whose blood coagulates abnormally rapidly (for example, it sometimes cannot be discharged from a 5 c.cm. syringe for a W. R.) are not to be recommended for giving blood for direct transfusion from vein to vein through special apparatus, as opposed to transfusion of citrated blood. Donors, part of whose blood is found coagulated in the bottle, should also be looked upon as risky for direct transfusion. Even when their blood is collected in a citrate solution and a clot has not formed immediately, trouble may arise later. This point should be remembered in giving transfusion to extremely anæmic cases whose blood is known to coagulate on coming into contact with normal blood in the presence of air (Greval and Chandra, 1939). The risk of coagulation will increase with a blood of high coagulability. From this point of view blood stored for at least 24 hours would be more suitable for such cases. Absence of coagula in it will rule out abnormally high coagulability.

The citrated blood should not be further diluted with saline outside the body as is sometimes done.

At times fine loose clots form in the bottle and choke the filtering end of the tube employed with a two-way syringe for transfusion. This difficulty is overcome by (i) keeping the filtering end of the tube just dipped in the blood or (ii) filtering the blood into another container and allowing time for the clots to drain. The clots when left to drain discharge most of the contained blood. Even a single massive looking clot is loose and discharges its blood when drained.

Incidentally, the concentration of sodium citrate recommended by the writers for preventing coagulation of blood is 0.25 per cent. It can be safely increased to 0.3 per cent by taking in the bottle 1/10th volume of the intended total a 3 per cent solution instead of 2.5 per cent, or even to 0.35 per cent by taking more than 1/10th volume of either solution. The limit of the salt allowed for an adult is 5 grammes.

#### 5. *Blood left in the collecting tube*

The tube between the vein and the bottle contains 5 to 10 c.cm. of blood (depending upon its length and calibre) when the stop-cock is closed. This quantity may be allowed to flow into the bottle slowly, without a rush of air with it, if the blood is to be used within half an hour or so. If the blood is to be stored it is better to reject this portion. The 'rejected' blood yields red blood cells and serum of known group for the routine of the laboratory. In fact the only utility of running a blood transfusion service from a laboratory is the regular supply of fresh red blood cells and sera of known groups. Samples of sera and red blood cells for direct matching of the stored blood with that of the recipient are also kept from this source. Handled with surgical precautions of asepsis and stored in the cold the cells and the sera keep almost fresh for ten days. The writers' limit of storage of blood for transfusion is also ten days.

#### 6. *Stoppering and labelling the bottle*

The bottle is stoppered by means of a glass stopper. The inner surface of the neck of the bottle is wiped with a sterile cotton swab if blood is seen on it. A flame is made to play on the surface and the ingoing portion of the stopper, as a matter of bacteriological etiquette. Melted hard paraffin which is just short of boiling, but has been boiled, is smeared liberally over the junction with a sterile swab. For opening a bottle so stoppered and smeared a flame is needed, which is an advantage.

The bottle is labelled by writing upon it with Indian ink. The writing is allowed to dry and then covered with a coat of collodion which is also allowed to dry.

The stoppering and labelling take about half an hour, which is the time needed for keeping the blood at room temperature if it is to be stored.

When the blood is taken from a particular donor for a particular recipient in a surgical theatre or a ward and is likely to be used up at once the need for stoppering and labelling the bottle does not arise.

#### 7. *Frothing of blood*

The blood froths if the negative pressure in the bottle is too high. The vacuum then should be slowly decreased.

Sometimes the froth is produced by air entering the needle through a faulty puncture in the

vein. A thrill in the rubber tube is then also felt. This is a serious fault and should be avoided by making sure that the needle has entered the vein fully in the first instance. For subsequent correction, advancement of the needle is indicated.

#### 8. *The tourniquet*

A tape tied round the upper arm as high as possible serves as a tourniquet. The pressure applied to reduce the size of the pulse is likely to abolish the pulse altogether if the subject passes into a state of fear. The tourniquet is then released and reapplied while measures are being adopted to reassure the subject. A partial state of fear with a slight fall of blood pressure is not incompatible with the commencement of the operation. The flow increases as the fear of the prick of the needle has been experienced and overcome.

When actual collapse has occurred no attempt to draw blood should be made.

An inflatable cuff such as is used with the sphygmomanometer, though more easily adjustable than the tape, restricts the field of operation and is not recommended. The operator should have an ample length of the vein and surface of the upper arm at his disposal.

#### 9. *Symptoms in the donor*

The symptoms essentially are those of collapse and occur in this order: (i) cold sweat, (ii) successive loss of colour from temples, forehead and cheeks, (iii) loss of consciousness, (iv) twitching of facial muscles, (v) convulsions (confined to limbs only), and, after recovery, (vi) dry mouth and (vii) unsteadiness.

The worst symptoms in the writers' experience have occurred *after the event*, in four cases, during the last three years. In three of them only 5 c.cm. of blood had been taken for grouping and testing the blood. The symptoms came after the puncture had been sealed. Probably the sight of blood in a glass container was responsible. Two subjects (male, Europeans) collapsed quietly while one (female, Indian) showed convulsions. From the fourth (male, European) 300 c.cm. of blood had been drawn. After the puncture had been sealed and the bottle of blood removed to another room he said softly 'I am dying', showed twitchings on face and convulsions in limbs. Face was bloodless and skin cold and clammy. He was at once placed in a horizontal position on his back (pulled down in the long chair which is used for bleeding donors) and constrictions round neck removed. Consciousness returned in less than a minute. Aromatic spirit of ammonia, one teaspoonful in a tablespoonful of water, was given. His hand holding the draught trembled and had to be guided to the mouth. Colour returned rapidly. Request for water was made but not much of it was drunk (dryness of the mouth disappeared rapidly). All was well

in about three minutes. Immediately afterwards the subject was wondering if he had fainted. In fifteen minutes he walked perfectly well to his ear. In thirty minutes he rang up to say that he was quite fit. Reports received morning and evening for two days over the telephone were of a perfect state of health.

Both the subjects showing convulsive movements and momentary loss of consciousness were suffering from domestic worries.

Subjects showing symptoms of collapse are not suitable for sending out as donors in cases of emergency.

Incidentally, women appear to be affected less than men by drawing of blood.

Of compensatory dangerous rise of blood pressure (Durand, 1939) after blood has been taken the writers have not seen a case. They do not attach any importance to it. They take blood for tests from patients and for transfusion from healthy donors. The annual number of venipunctures done in this laboratory was of the order of 200 two years ago. Since then it has been considerably increased. The increase is due to an increase in the donors of blood.

#### 10. Taking blood for serum from man and animals

Potain's aspirator can also be used for taking blood for immune serum from subjects convalescent from certain diseases, and from large animals of the size of or larger than sheep or goats, in quantities greater than the ordinary syringe will hold. The citrate solution of course will not be needed. Broken glass-rods in the bottle will aid in the coagulation of blood. The serum can be poured out carefully into another container, sucked and transferred with a sterile pipette or drawn with a two-way syringe as has been described in a previous communication (Greval and Chandra, *loc. cit.*).

#### 11. Cold storage of blood

(i) *The refrigerator.*—The writers use a gas refrigerator. Being free from vibration it preserves the red blood cells better than the ordinary electric refrigerator. The range of temperature available is 2°C. to 8°C. on the shelves. Along with the bottles of blood of groups O, A and B, separate samples of red blood cells and sera for direct matching are preserved. An electric refrigerator with its motor outside the cabinet can also be used. In localities where electricity or gas is not available a kerosene-operated refrigerator may be used. The range of temperature of this refrigerator is satisfactory.

(ii) *The period of utility of the preserved blood.*—Many opinions have been expressed within the last two or three years on the subject. Three rules of action emerge: (i) when the transfusion is needed for platelets, blood over 24 hours old should not be used; (ii) when the transfusion is needed for opsonins or leucocytes, blood over 48 hours old should not be used (Kolmer, 1939) but (iii) when a transfusion for red blood cells and complement (and

other constituents) is needed blood stored up to ten days can be used (Kolmer; Wiener, 1939; Editorial, *J. A. M. A.*, 1939). A suggestion is added that a transfusion also provides normal human proteins, immune bodies more stable than opsonins, hormones, enzymes, extractives, salts and ions; most of these constituents are likely to remain unaffected for weeks in the clear supernatant plasma of the stored blood. Even prothrombin left intact in the plasma has been found to be 61 per cent of the normal after three weeks (Lord and Pastore, 1939). This observation is important in view of using stored blood and plasma in hæmorrhagic conditions. A trace of colour from the underlying red blood cells is not likely to be harmful, at least from a bottle of the writers' stock (maximum content 400 c.cm.). Transfusion of compatible (exactly appropriate to the red blood cells or safe like the plasma of a safe universal donor) serum for most of the proteins and some of the other constituents is another undeveloped therapeutic measure. The serum may even be dried for the purpose of preservation and transport.

For most cases blood ten days old is suitable.

#### (iii) Decrease in food and allergic reactions.

—Such reactions amounting to fatal accidents are known to occur in transfusions even when compatibility of bloods and purity of the chemical used have been beyond dispute. They are due to unsuspected hypersensitiveness on the part of the recipient to the donor's blood. (Incidentally, the writers match sera also as a routine in determining compatibility, and recommend a scratch skin test in addition, when a donor serves on a recipient more than once.) This danger of food and allergic reactions is said to decrease with stored blood (DeBaakey and Honold, 1938).

(iv) *Advantage of further observation on the state of health of the donor.*—That a donor at the time of giving blood may be incubating an acute infective disease is a possibility especially during epidemics. The longer the blood is kept (up to ten days) the surer one is of the state of health of the donor. The writers keep in touch with the donors for a week.

Destruction of malaria parasites in preserved blood (Halbrecht, 1939) may not be relied upon. Blood containing parasites of monkey malaria has been sent for the propagation of the plasmodium from Calcutta to Hamburg by air mail and from London to New York by ship (private communication by Dr. B. M. Dasgupta of the School of Tropical Medicine, Calcutta).

(v) *Stored blood is not a second-rate therapeutic aid.*—From what has been said so far it is abundantly clear that under proper organization the stored blood is not inferior in utility to freshly drawn blood. In fact it is superior.

(vi) *Easy availability.*—The stored blood of a safe universal donor (all subjects belonging to group O, group I Jansky or group IV Moss, are not safe universal donors) for use in

emergencies, such as accidents or hæmorrhage in maternity cases, is available within minutes. It is better that for the purposes of issuing such blood the scope of an emergency is not allowed to go beyond the illustrations given. For a patient who can receive the blood of his own group the blood of a safe universal donor is an unnecessary and unfair handicap; and when the stored blood is used up in imposing the handicap, a life may be lost which could only be saved by its use.

(vii) *Increase in supply.*—By storing blood the number of donors is increased. A professional donor is not without other professions. To come and give blood to hospitals and nursing homes, mostly during working hours, he has to give up his own work. This inconvenience is liquidated by taking his blood at his convenience and storing it. Thus more donors become available and the donor's fee is reduced. Free donors also come forward. The Red Cross Blood Bank of Calcutta has on its list 30 free donors who come to donate blood every 6 to 8 weeks if necessary. When the Bank issues blood in exchange for relations' or friends' blood (which may not be compatible) two bloods are taken for one given. This results in further increase in donors. Prospective professional donors are also bled once free of charge, for storage, to get them used to bleeding. The blood might even be bought in anticipation of the demand when the demand could be anticipated fairly well. At present the Blood Bank (i) issues blood free for friendless and relationless indigent patients, (ii) receives two bloods for one given when friends and relations give blood, and (iii) receives from the well-to-do patients donations which are sent to the Red Cross Society. In the writers' opinion this plan suits the needs of Calcutta. During the last six months 34 bloods have been issued. During the same period 71 donors have been supplied by the Blood Transfusion Service of this laboratory (different from the Blood Bank).

(viii) *Blood in a rubber-capped bottle.*—For issuing small quantities of blood (up to 20 c.cm.) the bottle is capped, not stoppered. With sterile precautions, syringes are filled from it when needed. Blood for experimental purposes is always so kept by the writers.

(ix) *Human red blood cells are not so fragile as sheep's red blood cells with which most laboratory workers are familiar.*—The writers have received samples of blood from prospective recipients not living in Calcutta and Bengal for grouping, matching and supplying donors. The bloods have been brought by special messengers by train. The donors have been supplied. Besides packing the tubes of blood [(i) untreated whole blood for serum and (ii) citrated blood for cells] in a tin and the latter in ice, other devices for preserving by cold are a wide-mouthed 'thermos', dry ice and the refrigerated wagon of certain trains on certain days.

(x) *The writers' scheme of storing blood is different from the London Scheme of Blood Transfusion Service for War* (as published in the *Brit. Med. Journ.*, 1939, Vol. II, pp. 35 and 570).—The latter scheme stores blood of subjects of group O only. The writers store blood of subjects of groups O, A and B. A few donors of group AB are on the register and blood from them can be used for special recipients of group AB. Ordinarily recipients of group AB receive blood of other groups *after the danger of the isoagglutinins of high titre* has been eliminated. Further, the writers divide their subjects of group O into (i) safe universal donors of first choice, (ii) safe universal donors of second choice, and (iii) dangerous 'universal donors' (= merely group O donors for group O recipients). This important consideration of the titre of the isoagglutinins of the donors has been discussed at length in a previous communication (Greval and Chandra, *loc. cit.*).

#### 12. *Firms supplying apparatus*

Special stoppers for Potain's aspirator, two-way stop-cock and adapters can be obtained from Messrs. H. Mukerji & Co. of 39, College Street, Calcutta. The stop-cock can also be obtained from the Bombay Surgical Company, New Charni Road, Bombay.

It does not appear to be well known in India that Record syringes can be rebarrelled at a reasonable cost. The Bombay Surgical Company undertakes the repairs.

Kerosene-operated refrigerators are stocked by the Army and Navy Stores, Ltd., Calcutta.

#### *Summary*

1. The paper is a continuation of two recent papers on taking blood for transfusion.
2. The special stopper of Potain's aspirator and tubes can be autoclaved.
3. The blood taken, as described previously, can be stored.
4. The pump of Potain's aspirator is not essential.
5. Blood sometimes coagulates in the apparatus or the bottle. This is due to (i) obstruction in the tube and (ii) abnormally high coagulability of some bloods. Obstruction can be removed. High coagulability needs consideration when anæmic patients are to be transfused. The clot in the bottle can be drained.
6. Blood left in the collecting tube when the flow is stopped should not be run into the bottle if the blood is to be stored. The rejected blood provides material for work in the laboratory.
7. The bottles are stoppered with glass stoppers which are secured in place and made dust-proof with melted hard paraffin. They are labelled with Indian ink and the writing covered with a layer of collodion.
8. The blood froths in the bottle when the negative pressure is too high and when the whole of the aperture of the needle is not in the vein.

9. A tape is the best tourniquet for the purpose of bleeding a donor.

10. Symptoms in the donor are those of collapse. They are not serious. Women have suffered less than men. A compensatory dangerous rise of blood pressure has not been observed.

11. The same apparatus can also be used in taking blood for serum from man and animals.

12. Cold storage of blood. (i) A gas refrigerator is to be preferred to an electric one. (ii) Utility of preserved blood varies from 1 to 10 days depending upon the requirements of the case; for most cases it is ten days. (iii) Food and allergic reactions with stored blood are said to decrease. (iv) The risk of the incubation period of acute infective disease in the donor can be excluded. (v) Stored blood is not a second-rate blood. (vi) It is more easily available. (vii) By its use the total number of donors is increased. (viii) It can be stored in rubber-capped bottles for issuing small quantities. (ix) Human red blood cells are not so fragile as sheep's. Bloods of prospective recipients from outside Calcutta and even Bengal have been received, grouped, matched and donors supplied. (x) The writers' scheme of storing blood is different from the London Scheme of Blood Transfusion Service for War.

13. Names of the firm supplying the apparatus needed and undertaking repairs of syringes are given.

#### Acknowledgments

The organization for the cold storage of blood was made possible by collaboration with the Red Cross Society, Bengal Branch. Colonel Boyd, I.M.S., Officiating Surgeon-General, Bengal (1939), ex-officio member of the Society and Sir Upendra Nath Brahmachari, the Chairman, to whom the scheme was presented, provided the personnel and equipment. Colonel R. N. Chopra, I.M.S. (Retd.), Director, The School of Tropical Medicine, Calcutta, provided accommodation in the Carmichael Hospital for Tropical Diseases connected with the School.

Drs. (Mrs.) L. S. Ghose, W.M.S., D.R. Dhar, Honorary Deputy Physician, Medical College, Calcutta, and S. Sen Gupta of Carmichael Medical College Hospital, Belgachia, assist in the physical examination of the donors.

Dr. Eileen Macfarlane and Mrs. S. D. S. Greval, members of the Blood Transfusion Committee of the Society, are responsible for publicity especially in the European community.

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(Continued at foot of next column)

## THE BUFFER PRECIPITATION TEST FOR MALARIA (B. P. T.) ADJUSTED FOR LARGE-SCALE EXAMINATIONS

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In a previous paper (Wolff, 1939) I described a new serological test for the diagnosis of chronic malarial infection. The test is based on the precipitation of a protein fraction of the blood serum (euglobulin) by buffer solutions, as it can be shown that normal blood and malarial blood behave differently when mixed with such solutions. If a large set of buffer solutions, covering a range from 5 to 8.4, is used it will be seen that the precipitation in normal sera fades out round about 7.4 whilst the precipitation of malarial sera extends much further towards the alkaline side, and, as a rule, is of a higher intensity within the ranges in which normal sera also are precipitated. Since, for diagnostic purposes, it has been decided to lay more stress on the extension of the reaction towards the alkaline side than on the differences of intensity, I suggested dispensing with most of the solutions and simplifying the technique by the selection of two solutions only, namely, pH concentration 7.0 and 7.4. Such procedure seems to be simple

(Continued from previous column)

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#### ADDENDUM

16th August, 1940.—Since this communication was despatched on 22nd June, 1940, other workers' communications on the use of concentrated serum (Best and Solandt, 1940), liquid stored plasma and dried plasma (Pathological Society of Manchester, 1940) have become available. Due to the unusual delay in transit they were received in Calcutta on or about 16th July, 1940. An announcement over the radio concerning the use of plasma has also been heard.

In the writers' opinion the concentrated serum, liquid or dried plasma and dried serum dissolved in water should conform to the standard suggested for the safe universal donors.

As has been suggested by the writers the plasma and the serum will have their place in therapeutics. They will not, however, replace transfusion of whole blood.

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 Pathological Society of Manchester (1940). *Ibid.*, i, p. 827.



enough, but did not satisfy us fully, as the reading of the 'abridged' test is not as easy as the reading of the original test.

An attempt was therefore made to improve on the readability of the abridged test without impairing its reliability and simplicity.

The new technique differs from the old one in so far as a control tube has been introduced, which serves a double purpose. Firstly, it allows us to read by comparison, which is easier than direct reading when we have to deal with slight turbidities; and, secondly, it helps us to detect turbidities of sera which are independent of the buffer effect, and are apt to upset the reading if not detected.

In spite of the addition of a control tube, the test has remained as simple as before, as one buffer solution is used instead of the two solutions recommended before.

### TECHNIQUE

#### 1. Solutions

- (a) *Test solution*—
- |                              |    |              |
|------------------------------|----|--------------|
| Stock buffer solution pH 7.7 | .. | One part     |
| Glass-distilled water        | .. | Four parts   |
| Formalin                     | .. | 0.2 per cent |
- (b) *Control solution*—
- |                              |    |              |
|------------------------------|----|--------------|
| Stock buffer solution pH 7.0 | .. | One part     |
| Glass-distilled water        | .. | Four parts   |
| Normal saline                | .. | Five parts   |
| Formalin                     | .. | 0.2 per cent |

The stock buffer solution pH 7.0 and 7.7 may be prepared either from Baird and Tatlock's Universal buffer mixture or by mixing acid potassium phosphate with sodium hydroxide according to Clark and Lub's formula for the preparation of phosphate buffers. These stock solutions have to be tested before use. They keep even in a hot climate for a considerable time if 0.2 per cent of formalin is added.

#### 2. Blood

The blood should be taken by venipuncture, and, if possible, in the morning before breakfast. About 2 c.cm. of blood is sufficient. It has to be placed in a dry and clean test tube or centrifuge tube. After clotting, the clot is loosened carefully with a glass rod from the wall of the tube, and the sample put in the refrigerator (or a cool place) overnight. The next morning the serum is ready for the test if well separated and clear; if badly separated or turbid gentle centrifuging may be done. The serum is not removed from the clot till it is added to the solutions during the actual test.

#### 3. The actual test

Test tubes 4 inches by half an inch are placed in two rows in a rack, the front row for the test solution and the back row for the control solution. For each serum one tube of each solution is required so that each row contains as many tubes as the number of sera to be examined. The solutions are distributed over these tubes in quantities of  $\frac{1}{2}$  c.cm. for each tube. One graduated 5 c.cm. pipette may be

used without harm for the distribution of both the solutions.

About 4 drops of serum are removed from the blood sample and two drops placed in each of the two test tubes. The most practical are Dreyer's drop pipettes with rubber teats. The same pipette can be used for all the samples if carefully rinsed with distilled water after taking each sample.

After the addition of the serum the tubes are shaken and left standing on the table at room temperature.

#### 4. The reading of the test

The reading may be done from half an hour to two hours after the completion of the test. The average positive case can be read almost immediately after the addition of the serum; but weakly positive cases develop slower, and for this reason it is advisable to wait 30 minutes before attempting the reading. Usually very small changes take place between 30 and 120 minutes, and there is no need to be specially careful as regards the exact time of reading.

The reading is best done by daylight. The two tubes belonging to the same sample are held side by side against the window, part of the window-frame providing a background. The light should not be too bright. Artificial light can be used instead, but care has to be taken that the light falls from a higher level from behind on to the tubes.

The reading is based on the comparison of the test tube and the control tube, and, in an average case, should present no difficulties. In most cases the control tube is quite clear and therefore even a delicate turbidity in the other will show up very well. Originally turbid sera show some turbidity in the control tubes, and the difference of the intensity of the turbidities has to be taken into account. Occasionally very strongly positive sera (hyperflocculating sera) tend to precipitate in the control tube to some extent, but always considerably less than in the actual test tube.

It is difficult to give hard and fast rules for the recording of the results. I suggested for the original test the following classification: 'opalescent', 'faintly cloudy', 'cloudy' and 'markedly cloudy', or 'plus-minus', 'one plus', 'two plus' and 'three plus'. For the modified test it may be found more convenient to call the very faint reaction (i.e., a turbidity just noticeable when compared with a clear control) 'doubtful' and the following grades of turbidity 'weakly positive', 'positive', 'strongly positive' and 'hyperflocculating'.

### DISCUSSION

#### 1. Limitations

Generally speaking, the simplified B. P. T. has the same limitations as the other serological tests for malaria described so far (Tyagaraja, 1938). This is bound to be the case as the



reaction cannot claim to be 'specific'. Incidentally, no such claim can be made for any of the serological tests for syphilis, which nevertheless are undoubtedly of the greatest value. In addition to the lack of 'specificity', which may occasionally interfere with the correct valuation of the positive readings, there are some difficulties in the reading of the test to be expected when we are dealing with 'boundary cases'. The reaction may become so weak that doubts must arise whether we should call it 'positive' or take shelter under the term 'doubtful'. This again is a well-known experience with all kinds of serological tests. On the other hand, difficulties arising out of such doubts may often be overcome by repeating the test at a later date.

## 2. Usefulness

In spite of these limitations, the usefulness of these tests seems to me well established. There is only one other disease that gives us positive results so regularly as malaria, namely, kala-azar, but, as a rule, the reaction in kala-azar is very much stronger, and a 'typical' malarial and a 'typical' kala-azar reaction differ considerably. The 'typical' kala-azar reaction is the hyperflocculation, i.e., the type of reaction in which a heavy precipitation forms almost instantaneously and settles quickly at the bottom of the tube; whilst the 'typical' malarial reaction does not show this very striking phenomenon. Still, we may come across such a reaction occasionally in malaria also (and possibly in some advanced condition of disturbed liver function); and in such cases an attempt should be made to eliminate or verify the diagnosis of kala-azar by the performance of the formol-gel test. In Ceylon, where kala-azar is unknown, this problem does not arise, and we have to pay attention only to the possible interference by liver disturbances when we come across 'hyperflocculation'.

The value of negative tests seems to be extremely high, provided, firstly, that the result is confirmed by a second test at a later date, and, secondly, that the blood is taken at the right time. The acute feverish period of a malarial attack has to be avoided, as we know that such an attack considerably diminishes the strength of the reaction, and reduces it even to *nil* if it has not reached a certain height before the test.

## SUMMARY

The simplified B. P. T. for malaria is performed with one test solution and a control solution.

The test solution is a diluted stock buffer solution pH 7.7.

The control solution is a diluted buffer stock solution pH 7 with the addition of normal saline.

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## OBSERVATIONS ON THE DIFFERENTIATION OF *BACT. COLI* AND *BACT. AEROGENES* ON LEVINE'S SIMPLIFIED EOSIN-METHYLENE-BLUE-AGAR AS APPLIED TO THE BACTERIOLOGY OF WATER IN BENGAL

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ESCHERICH originally observed the occurrence of two types of lactose-fermenting intestinal bacteria which are widely distributed in water and soil. One type *Bact. coli* was chiefly an inhabitant of the mammalian intestines and was thus regarded as the 'microbe of indication' of faecal pollution of water and the other type *Bact. aerogenes* was rare in human faeces but constituted the predominating coliform organism of soil and grain. Our regular procedure in this laboratory, for the bacteriological examination of water, is based on orthodox British practice, and MacConkey's neutral-red bile-salt lactose agar plates are almost universally used throughout India for confirmation of 'presumptive tests' for *Bact. coli*. The difference between these two types of coliform organisms on MacConkey's solid medium has been observed to be neither so clear-cut nor so distinct as to enable easy differentiation on plates. Another valuable medium—eosin-methylene-blue-agar—was first described by Holt-Harris and Teague for the isolation of the typhoid group of organisms from faeces. Levine (1918) modified this medium as follows:—

Distilled water	..	..	1,000 ml.
Peptone (Difco)	..	..	10 gm.
Di-potassium hydrogen phosphate	..	..	2 gm.
Agar	..	..	15 gm.
Lactose	..	..	10 gm.
Eosin yellow, 2 per cent	..	..	20 ml.
Methylene blue, 0.5 per cent	..	..	20 ml.

He claimed the possibility of easy differentiation between two types of coliform organisms by direct inspection of colonies grown on his modified medium. His results recorded on 52 cultures obtained from eosin-methylene-blue-agar after preliminary enrichment in lactose broth are shown in table I.

(Continued from previous column)

The test takes very little time, and no special outfit is required. It is kept at room temperature and may be read within half an hour.

The usefulness of the test is almost the same as of the original B. P. T. Its simplicity makes it more suitable for routine work on a large scale.

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TABLE I

From appearance of colonies on plates	Number of cultures	Number correctly designated	Per cent confirmed
1. Tentatively regarded as <i>Bact. coli</i> .	26	24	92.4
2. Tentatively regarded as <i>Bact. aerogenes</i> .	26	26	100.0

These results clearly showed that it might be possible to differentiate between *Bact. coli* and *Bact. aerogenes* simultaneously, confirming the 'presumptive test' for *Bact. coli* by inspection of colonies grown on the plates. The author, however, seems to have tested the culture with Voges-Proskauer (V. P.) and methyl-red (M. R.) reactions.

Recent investigations by Pawan (1925), Hicks (1927) and Taylor (1927) have rendered it evident that the *Bact. coli* standards are not strictly applicable to tropical water supplies. Under tropical conditions a fairly large proportion of organisms conforming to the reactions M. R. positive and V. P. negative of *Bact. coli* are found in water which, from a sanitary survey, should be regarded as relatively free from faecal contamination. Many of these organisms belong to a group of strains which appear to occupy a position, which is in some respects intermediate between *Bact. coli* and *Bact. aerogenes* types. The distribution of the latter types of organisms, however, is similar to that of *Bact. aerogenes* and their presence in water cannot evidently be regarded as indicative of dangerous faecal pollution. It has also been made sufficiently clear that the examination of lactose-fermenting organisms for the M. R. and V. P. reactions does not afford a sufficient basis, especially under tropical conditions, for forming a conclusive opinion. It is thus felt desirable to employ Koser's (1926) citrate utilization test and other biochemical tests for the purpose.

Moreover, methylene blue, an ingredient employed in the preparation of this medium, was first used in 1885 by Ehrlich as an indicator for biochemical reductions. Recently in 1932 Lindsey and Meckler claimed to have applied successfully the methylene-blue reduction test for differentiating *Bact. coli* from *Bact. aerogenes* types of coliform organisms. Raghavachari and Iyer (1935), however, applied this test to over two thousand cultures from waters and faeces at Madras and concluded that the claim relating to uniform reduction of dye by 100 per cent of an *aerogenes* group, made by previous authors, could not be confirmed.

Thus, in the light of our recent knowledge, as indicated above, assessing especially the proper significance of the intermediate types in tropical countries, it was thought highly desirable to undertake further work to refute or corroborate the results recorded by the previous author on the use of his simplified eosin-methylene-blue-agar. No such results, however, appear to have been recorded in Bengal.

The colonies grown on the eosin-methylene-blue-agar plates after 48 hours incubated at 37°C. from samples of water and faeces, after preliminary enrichment in MacConkey's broths, fall into four types:

(1) Small, 1 to 2 mm. in diameter, transparent or amber-coloured colonies. These are usually of intermediate group of cholera-typhoid (non-lactose-fermenters).

(2) Medium-sized colonies, 3 to 4 mm. in diameter, slightly raised, surface flat or slightly concave, having dark almost black centres which extend more than three-quarters across the diameter of the colonies, by transmitted light; button-like, often concentrically ringed with greenish metallic sheen with no tendency to run together. These are usually colonies of *Bact. coli* (types 1 and 2) but they not infrequently contain strains of intermediate types.

(3) Large colonies, 4 to 6 mm. in diameter; considerably raised and markedly convex; occasionally the centre drops down precipitately, centres brown or pale brown, smaller in proportion to the rest of the colonies with no metallic sheen in reflected light except rarely in the depressed centres. These are usually *Bact. aerogenes* or intermediate types.

(4) Red colonies, 1 to 2 mm. in diameter. They are generally cocciform and atypical or irregular lactose-fermenters.

In the first series of experiment 31 pure cultures of *Bact. coli*, *Bact. aerogenes*, intermediates (coliform) and members of typhoid and paratyphoid groups were plated on this medium for the purpose of differentiation and the results obtained are shown in table II.

TABLE II

Number of colonies tested	Types of bacteria	NUMBER OF COLONIES GIVING CHARACTERISTIC APPEARANCE		
		<i>Bact. coli</i>	<i>Bact. aerogenes</i>	Member of typhoid group
10	<i>Bact. coli</i> types 1 and 2	9	1	Nil
7	<i>Bact. aerogenes</i> types 1 and 2.	Nil	7	Nil
10	Intermediate types 1 and 2.	7	3	Nil
4	Typhoid and paratyphoid group.	Nil	Nil	4

From the above results it is evident that all types of bacteria generally gave characteristic reactions on this media except some of the intermediate types.

With a view to determining the degree of accuracy and reliability of the plate method of differentiation, 966 colonies were picked from eosin-methylene-blue-agar plates after incubation for 48 hours (the differences of colonies after incubation for 24 hours were not very distinct). They were grown from 40 samples of water

collected from various sources, after preliminary enrichment in MacConkey's broth. They were tentatively designated as *Bact. coli* or *Bact. aerogenes* types from their appearances on the plates. These designations were then checked by identifying the colonies on culture with the usual differential tests—indol production, M. R., V. P., Koser's citrate and fermentative reactions of sugars, lactose, saccharose, dulcitol and adonitol. The results of 642 colonies tentatively regarded as *Bact. coli* are shown in table III.

From table III it is seen that 483 (75.2 per cent) out of 642 colonies, tentatively regarded as *Bact. coli*, could be confirmed. One hundred and nineteen colonies (21.6 per cent) were found to be intermediate types and 20 colonies (3.2 per cent) were *Bact. aerogenes* types. It should also be noted that 96.8 per cent of the total number of colonies tested were M. R. positive. Evidently, if all the colonies giving positive reactions to M. R. are classed as *Bact. coli*, the percentage of colonies confirmed would have been approximately as high as those observed by Levine. But 21.6 per cent of them had been identified as intermediate types by Koser's citrate-utilization test.

per cent of the colonies were positive to the citrate test and could be thus eliminated. 28.8 per cent of them, however, were found to be positive to the M. R. test also.

#### Summary

The relative significance of the common types of lactose-fermenting bacteria found in tropical waters has been reviewed with special reference to the intermediate types.

Levine's modified eosine-methylene-blue-agar has been employed with a view to differentiating *Bact. coli* and *Bact. aerogenes* simultaneously for confirming the 'presumptive coli' by inspection of colonies on the plates. Nine hundred and sixty-six colonies were tested in this way and the results show that the differences between these two types of colonies could often be made out after incubation for 48 hours, but the less significant intermediate types could not always be eliminated. Out of 642 colonies, tentatively regarded as *Bact. coli*, from their appearances on agar, 483 colonies (75.2 per cent) could be confirmed as such by differential tests, 22.6 per cent were found to be of intermediate types and 3.2 per cent were of *Bact. aerogenes* types. Out

TABLE III

Type of organism	DIFFERENTIAL TESTS USED					PERCENTAGE			
	Indol.	V. P.	M. R.	Growth in citrate	Number of each type of bacteria	Each type of bacteria	Colonies giving reactions		
							M. R. +	V. P. +	Citrate +
<i>Bact. coli</i> type I ..	+	—	+	—	462	71.9	..	..	..
<i>Bact. coli</i> type II ..	—	—	+	—	21	3.3	..	..	..
Intermediate type I ..	+	—	+	+	96	14.9	96.8	3.2	24.8
Intermediate type II ..	—	—	+	+	43	6.7	..	..	..
<i>Bact. aerogenes</i> type I ..	+	+	—	+	18	2.8	..	..	..
<i>Bact. aerogenes</i> type II ..	—	+	—	+	2	0.4	..	..	..

TABLE IV

Type of organism	DIFFERENTIAL TESTS USED				Number of each type of bacteria	PERCENTAGE			
	Indol.	V.P.	M. R.	Growth in citrate		Each type of bacteria	Colonies giving reactions		
							M. R. +	V. P. +	Citrate +
<i>Bact. aerogenes</i> type II ..	—	+	—	+	215	66.3	..	..	..
<i>Bact. aerogenes</i> type I ..	+	+	—	+	16	5.0	..	..	..
Intermediate type II ..	—	—	+	+	55	17.0	28.8	71.3	92.9
Intermediate type I ..	+	—	+	+	15	4.6	..	..	..
<i>Bact. coli</i> type II ..	—	—	+	—	17	5.2	..	..	..
<i>Bact. coli</i> type I ..	+	—	+	—	6	2.0	..	..	..

From table IV it is apparent that out of 324 colonies tentatively regarded as *Bact. aerogenes*, 231 (71.3 per cent) could be confirmed as *Bact. aerogenes* types, 70 (21.6 per cent) were of intermediate types and 21 (7.2 per cent) were of *Bact. coli* types, and it is significant that 92.9

of 324 colonies tentatively regarded as *Bact. aerogenes*, 231 (71.3 per cent) could be confirmed as *Bact. aerogenes* types, 70 (21.6 per cent) were of intermediate types and 21 (7.2 per cent) were of *Bact. coli* types.

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# VIBRIO CHOLERÆ AND OTHER VIBRIOS

(OBSERVATIONS ON 'WATER VIBRIOS', WITH SPECIAL REFERENCE TO THEIR VARIATION DURING STORAGE IN CULTURE MEDIUM AND POSSIBLE RELATIONSHIP TO *Vibrio cholerae*)

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TOMB and MAITRA (1926) as a result of their investigations concluded that the agglutinable vibrio found in the dejecta of cholera patients, and the non-agglutinable vibrio found in carriers and in natural waters contaminated with human faeces are one and the same organism. They arrived at this conclusion after inseminating tanks\* with fresh cholera stools containing large numbers of agglutinable vibrios and examining the water at two-hour intervals. They state that between the 12th and 20th hour all the agglutinable vibrios from the stools had changed to non-agglutinable.

d'Herelle, Malone and Lahiri (1930) have stated that inagglutinable vibrios found in nature originated from typical cholera vibrios and suggested that the mutation which they have undergone had been produced by the action of bacteriophage.

d'Herelle (1930) in dealing with the epidemiology of cholera has brought forward ample evidence to show that vibrios isolated from convalescent cholera cases are probably avirulent and suggest that this loss of virulence is the result of bacteriophage action.

## *Cholera vibrio mutants produced by the action of cholera phage types*

Early in 1935, when 11 definite types of cholera phage had been isolated, a cholera

\* The word 'tank' used in the paper means a large pond or reservoir, either natural or artificial.

(Continued from previous page)

Thus the confirmation of the 'presumptive tests' for *Bact. coli* on Levine's eosin-methylene-blue-agar in the bacteriological examination of water under the conditions existing in Bengal should not be considered as strictly reliable, but may be very conveniently adopted for 'partially confirmed tests'.

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vibrio, strain 653, which was the only strain in this Institute that was lysed by all the then known types, was made resistant to all but one type of cholera phage. Thus 12 resistant cultures were prepared and these were labelled 11-A<sup>r</sup>, 11-B<sup>r</sup> and so on to 11<sup>r</sup>.

11-A<sup>r</sup> culture was that which was made resistant to B, C, D, E, F, G, H, J, K, and L types of cholera phage and hence only 'A' type lysed it. The 11<sup>r</sup> was one which was made resistant to all the 11 types of cholera phage. The biochemical and serological reactions, etc., of these cultures were then tested.

**Sugar reactions.**—Ten out of the twelve variants gave sugar reactions of Heiberg (1936) type I. The two variants which gave different reactions were 11-D<sup>r</sup> and 11-H<sup>r</sup>.

For the first 48 hours 11-D<sup>r</sup> gave the sugar reactions of type VI, but after 7 days there was slight acidity in saccharose only (type II). 11-H<sup>r</sup> after 7 days showed slight acidity in mannose only (type V).

**Colony appearance.**—The most marked change noticed was in the size of the colonies as compared with those of the parent strain. Some variants, on being plated, produced minute colonies, even after the plates had been incubated for 48 hours.

**Serological reactions.**—High titre sera (H + O) were prepared by injecting rabbits intravenously with living cultures of each of the 11-1<sup>r</sup> and the 11<sup>r</sup> variants\*, and cross agglutination tests were carried out. Formolized saline suspensions were used. Parent 653 (H + O) serum only agglutinated four variants to a titre of 50 per cent or over. Four out of eleven variant sera did not agglutinate the parent culture up to 50 per cent of their titre. Some variant cultures were agglutinated by one or two of the 12 sera, up to 100 per cent of titre.

## Example

Strain	Sera agglutinating to 100 per cent	Other sera
11-D <sup>r</sup>	11-D and 11-K	From 0.0 to 50 per cent.
11-J <sup>r</sup>	11-J	" 2.5 " 25 "
11 <sup>r</sup>	11-J and 11 <sup>r</sup>	" 2.5 " 50 "

In view of these preliminary findings with laboratory-produced variants, the question arose whether the observations reported by Tomb and Maitra were due to the action of cholera phage in the water on the cholera vibrios.

In addition to studying the characters of the 11-1<sup>r</sup> variants, other resistant cultures were prepared from the same parent 653 cholera vibrio by subjecting it to the action of one type of cholera phage. The single resistant secondary

\* No serum could be prepared from 11-E<sup>r</sup> culture as this culture became resistant to E type phage.

cultures all gave the sugar reactions of Heiberg type I and all were agglutinated to over 50 per cent of titre by the parent H + O serum. This bears out d'Herelle's (1926) earlier statement that the loss of agglutinability with specific serum is related to the degree of acquired resistance to phage. Mention of the above findings is made in the report of the Cholera (Bacteriophage) Enquiry at Shillong (Russell, 1935).

#### 1936 investigation

An opportunity was afforded in 1936 to investigate whether any relationship exists between the non-agglutinating vibrios isolated from water and phage-resistant variants of a true cholera vibrio produced in the laboratory. In that year a Field Research Laboratory, which was equipped by the Pasteur Institute, Shillong, and financed by the Indian Research Fund Association, was sent to Habiganj, a subdivision of the Sylhet District. The functions of this laboratory were to investigate epidemic and sporadic cases of cholera, carrier cases and vibrios isolated from river and tank waters in the district. The field laboratory carried on this investigation for one year. After a preliminary examination in the field laboratory, all vibrio strains isolated were sent to this Institute for further examination. In addition to the usual biochemical and serological tests, the writer tested all the water vibrios received for phage lysability with the 11 types of cholera-phage and for agglutination against the 11-1 resistant sera which had previously been prepared, and also against Inaba and Ogawa 'O' sera. The results of the investigation carried out during 1936 are summarized below:—

One hundred and fifty-nine strains of water vibrios were examined.

**Fermentation reactions.**—With the exception of three, all the strains which showed lysis with any of the cholera-phage types, or which were agglutinated by any of the 11-1 sera (H + O) belonged to Heiberg's fermentation types I, II and V. The three exceptions belonged to Heiberg's type III. A further reference will be made to these three strains in the next section. Two other strains were agglutinated by Inaba 'O' serum to 50 per cent of titre, but these were neither lysed by any of the cholera-phage types nor agglutinated by any of the 11-1 sera.

**Agglutination and phage reactions.**—Twenty strains were agglutinated by one or more of the 16 sera used, up to 50 per cent of titre or higher.

The parent 653 serum only agglutinated six of these.

Fourteen of the 159 strains were lysed by one or more of the phage types, and 12 of these were agglutinated by the variant sera. No strain was agglutinated by Ogawa 'O' serum.

During the course of the above investigations, and after the preparation of the H + O variant sera, the importance of 'O' agglutination in the classification of vibrios began to be stressed.

The writer therefore decided to re-examine, as many of the above cultures as possible for 'O' agglutination, and at the same time to re-test their sugar reactions and phage lysability.

#### 1937 investigations

Preliminary investigation into laboratory-produced variants:—

In 1936 a new type of cholera-phage, namely 'M', was described by Pasricha *et al.* (1936). A sample of this phage was very kindly sent to this Institute by Major Pasricha. Before preparing the series of 'O' sera, all our 11-1 phage-resistant cultures were made resistant to the new phage type. High titre 'O' sera\* were prepared from all but 12-C<sup>r</sup> variant, as no satisfactory high titre serum was obtained against this strain. In addition to the 12 variant sera, 'O' sera were also prepared from the parent strain 653 and from Inaba (Rough). The object of including Inaba (Rough) serum was to ascertain whether any agglutination which might occur with any of the other sera was due to the rough factor. Thus in all 16 'O' sera were employed, comprising the 12 prepared from the phage-produced variants, one each from the parent strain 653 and Inaba (Rough) and the two stock laboratory 'O' sera Inaba and Ogawa. The titre of most of the sera was 1 in 1,000, but in a few instances a maximum titre of 1 in 500 could only be obtained.

Before re-testing the 1936 cultures, the biochemical and agglutination reactions of the 12-1<sup>r</sup> cultures were tested. After 48 hours all variants with the exception of the following gave the reaction of Heiberg's type I:—

Variant cultures	Heiberg's type
12-B <sup>r</sup> ..	V
12-D <sup>r</sup> ..	II
12-E <sup>r</sup> ..	II
12-L <sup>r</sup> ..	II

These variants (each lysed by one type of cholera-phage and agglutinated by at least one variant serum-homologous) have therefore given similar results to those water vibrios which in the 1936 enquiry were agglutinated by variant sera or were lysable by cholera-phage. They all belonged to Heiberg's type II or V.

Nine of the cholera vibrio variants were tested against 'O' sera prepared from cholera strains Inaba (Smooth), Ogawa, 653 and Inaba (Rough).

\* These sera were prepared from suspensions of 24 hours' old agar cultures in normal saline. The suspensions were placed in a boiling water-bath for two hours.

The results are summarized below :—

'O' serum	Strains agglutinated to 100 per cent of titre	Other strains (percentage agglutination)
653 ..	12-A	0 to 25.0
Inaba (Smooth) ..	12-J	25 „ 50.0
Ogawa ..	12-A	0 „ 12.5
Inaba (Rough) ..	Nil	5 „ 50.0

Although the parent strain belongs to the Ogawa group, Inaba (Smooth) serum agglutinated the variants better than either parent 653 or Ogawa sera.

The results obtained with Inaba (Rough) serum do not suggest that the predominant change produced by phage action on the vibrio is one from smooth to rough. If this were so, one would expect these variants to be agglutinated in higher dilutions than the results shown above.

The next step was to test some of the variant 'O' sera against cholera vibrio strains 653, Inaba (Smooth), Ogawa and Inaba (Rough). The results obtained are shown in the following table :—

TABLE

Serum	Titre	CHOLERA VIBRIO STRAINS. PER CENT OF TITRE TO WHICH AGGLUTINATED			
		Inaba (Smooth)	653	Ogawa	Inaba (Rough)
12-A <sup>r</sup>	1 in 1,000	12.5	100.0	50	0.0
12-G <sup>r</sup>	1 in 500	25.0	25.0	10	100.0
12-H <sup>r</sup>	1 in 1,000	12.5	12.5	5	25.0
12-K <sup>r</sup>	1 in 1,000	12.5	12.5	5	12.5

These results confirm the above findings, showing that except 12-A<sup>r</sup> variant, the others have markedly changed in their antigenic properties and in only one (12-G<sup>r</sup>) can the change be ascribed to that of roughness.

#### Re-examination of the 1936 cultures

All the vibrios examined during 1936 were stored as agar stab cultures, the test-tube plugs of which were waxed. These were stored at room temperature (4°C. to 26°C.) for a period of from 9 to 12 months. When required for re-testing, each strain was subcultured on to three agar slopes and another stab was made which was kept in stock. Formolized saline suspensions were prepared for agglutination from two 24-hour cultures and the third slope was used for the sugar reactions and for the phage lysability test. Seventy strains in all, selected from the various Heiberg's types, as classified in 1936, were examined. Four of these, as shown below, were agglutinated by one or more of the variant sera up to 50 per cent of titre.

#### Agglutination reactions

Sugar reactions (1936). Heiberg's types	Strain	Sera by which agglutinated
I	W. 27	12-G, 12-H, 12-K
II	W. 116	12-H (trace agglutination from 1 in 50 to 1 in 500).
III	525	12-D, 12-II, 12-K
VI	W. 11	12-K

No strain belonging to type IV or V was agglutinated. Under the 1936 investigation mention has been made of three strains which belonged to Heiberg's type III which were lysed by one or more phage types and which were agglutinated by variant sera. These strains were 525, 525(1) and 525(2). When these were re-tested in 1937 they all gave the sugar reactions of type I. An unusual finding was strain W.11, which belonged to type VI, but which was agglutinated by 12-K serum. This strain was investigated further in 1938, and a possible explanation of the present finding is given under the 1938 investigation.

**Sugar reactions.**—When re-tested it was found that the fermentation reactions of a large number of strains had altered. This change was noticed in all the Heiberg's types. Some from type I had changed to type II; others from type II had changed to types I, III and IV, etc. In spite of these changes, it was again noticed that those strains, which on re-testing were lysed by one or more types of cholera phage gave the sugar reactions of Heiberg's type I, II or V. It should be mentioned here that a typical cholera vibrio was always sown in a duplicate set of sugar tubes whenever a batch of water vibrios was tested for their fermentative reactions. The control invariably fermented saccharose and mannose but not arabinose.

**Phage lysability.**—Of the strains re-tested, ten were originally lysed by one or more cholera-phage types. In 1937, nine of these were again tested and the strains were lysed by more phage types than originally. One strain (373) which in 1936 was lysed by 'J' type phage, was found to be resistant to all types in 1937. Later (1938), however, it was lysed by G, H and J types. Four additional strains which were resistant to all types in 1936, were in 1938 lysed by one or more types. Similar loss of resistance to phage types has repeatedly been noticed among our 12-1 resistant cultures when stored for some months as agar stab cultures. For instance, a 12-A resistant culture is tested and found to be lysed by 'A' type cholera phage only. It is then stored for some months as an agar stab culture with the test-tube capped and waxed. When re-tested later it has often been found that, in addition to being lysed by 'A' phage, the culture had lost its resistance to one or more of the other types of phage. The



probable explanation for this may be found in the following statement made by d'Herelle and Rakieten (1934):—

'One of us (d'Herelle) has shown experimentally that the general behaviour of any natural symbiosis found in nature is realized in the case of bacterium-phage symbiosis. Three types of process may take place. The bacteria may be destroyed if the virulence of the phage increases; symbiosis may persist indefinitely if the phage virulence and the bacterial resistance are balanced, or the phage may be destroyed if the resistance of the bacteria increases. The result in the third instance is a phage-free bacterium'.

It is to the third process that the loss of resistance described above must be attributed. As the bacteria are infected by phage it is only natural that these are constantly striving to throw off this infection and if these vibrios do finally, by increased resistance, rid themselves of the infection of each and every type of cholera phage by which they were attacked, they would revert to a phage-free vibrio.

#### *Investigations on recently isolated strains*

In addition to the 70 strains already dealt with above, 72 more strains, which were freshly isolated from various samples of water by Dr. S. R. Pandit, Officer-in-Charge of the Cholera Enquiry at Shillong, were examined by the writer for phage lysability and in some cases also for agglutination. The sugar reactions were carried out by Dr. Pandit. Seven strains were lysed by phage types, details of these are given below:—

Strain number	Heiberg's types	Lysis by cholera phage types
739/2/1	V	B. F.
739/2/2	II	H.
704/1/1	II	J. M.
704/1/2	II	J. M.
704/2	II	J. M.
730/1/3	V	B. C. F. K.
730/2	V	B. C. F. K.

*Agglutination reactions.*—These seven strains were tested against the 16 'O' sera. Only one strain (739/2/2) was agglutinated to 100 per cent of titre by 12-D and 12-H sera. If we add these seven strains, which belong to Heiberg's type II or V to those mentioned in the 1936 investigation, we have a total of 21 strains susceptible to phage action. They all belonged to Heiberg's type I, II or V. As previously mentioned, four more strains, which were originally resistant, were lysable in 1937, three belonged to type II and one to type V.

Therefore out of a total of 231 strains which were tested or re-tested during 1936 and 1937, 25 were lysed by cholera phage and all belonged to Heiberg's type I, II, or V. The remaining 206 phage-resistant strains belonged to type III, IV or VI.

#### *1938 investigation*

Owing to the number of strains which were found to have altered in sugar reactions and in order to confirm these findings, some of the original strains, which had again been stored as agar stab cultures after they were investigated in 1937, were re-examined for their fermentative reactions in 1938. These had been stored for a further period of from 4 to 6 months since they were re-tested in 1937. Many of the strains had again altered in their sugar reactions. Some had reverted to their original Heiberg type, others which had changed when re-examined in 1937, still gave the 1937 reactions, while others gave reactions different to those obtained in 1936 and 1937. An example of these findings is given.

Strain	Fermentation reactions Heiberg's types		
	1936	1937	1938
227(2) ..	I	II	I
210(1) ..	III	IV	IV
542 ..	VI	III	IV

After another 2 months a final examination was made of those vibrios which had previously been either lysed or agglutinated. This time, however, each strain was subcultured from the agar stab culture into peptone water and was subcultured daily for 4 days in this medium. Each culture was then plated and four smooth translucent colonies were picked off and inoculated into papain-casein broth (Vardon and Datta Roy, 1938). Daily passages in this medium were made for 4 more days. Each of the four broth cultures was next transferred to agar slopes and these agar cultures were used the next day for lysability, sugar reactions and agglutination tests. Changes in reaction, as shown below, were again noticed. The reactions under 1938 are given as (1) and (2), the former refers to the first 1938 examination and the latter to the final one.

Strain	Heiberg's types			
	1936	1937	1938 (1)	1938 (2)
27	I	I	I	V
116	II	I	II	I
373	II	V	V	II

All four colonies tested invariably gave identical sugar reactions.

turned to the products of intestinal putrefaction such as phenols and aromatic oxyacids, which are highly toxic and which are found in the blood and cerebro-spinal fluid of uræmic patients in concentrations varying with the intensity of symptoms. Moreover, it has been pointed out by Volhard and Becher (1929) that these toxic phenols can find their entrance into the cerebro-spinal fluid only when some structural alterations have rendered the choroid plexus permeable, either as a result of damage brought about by kidney failure or some gross anatomical change superimposed on it. Changes in the choroid plexus had been reported by Von Monakow as early as 1920. The senior writer has personally seen two cases of uræmia in which the choroid plexus showed definite anatomical change and in at least one there were large and small cystic dilatations in the organ making it look like a bunch of grapes. Unfortunately difficulty in obtaining a larger number of autopsy examinations has stood in the way of further confirmation of the above observations.

All recent work tends to support the view that uræmia is a clinical syndrome produced either by a chemical disturbance in the blood and tissue fluids owing to a high grade renal failure, or a physical disturbance of the intracranial circulation associated with hypertension. In many instances both the factors may be at work in the causation of uræmia. The first condition is nowadays regarded as true uræmia or chronic retention uræmia and the second is designated as pseudo-uræmia or acute convulsive uræmia known as hypertensive encephalopathy of Fishberg. From a study of the varying symptomatology of chronic retention uræmia and also of all the experimental work on that line, it appears that uræmia is not due to the retention in the blood and tissues of any one particular chemical agent, but to the alteration in the relative amounts of several substances. These variations may differ considerably from one case to another. For instance, as a result of renal failure, there is not only a retention of the various non-protein nitrogenous constituents but also of a considerable amount of inorganic phosphates, with diminution in the available ionized calcium in the blood and cerebro-spinal fluid. Moreover, an accumulation of guanidine and phenol derivatives has been observed in the blood. Last but not least important are the dehydration, acidosis and chloride deficiency, which, though not essential features of the uræmic syndrome, are present in many cases associated with vomiting and diarrhœa.

A proper appreciation of these biochemical changes would be very helpful in the interpretation of the varied clinical pictures of true uræmia. Thus retention of inorganic phosphates with diminution in the ionized calcium, especially in the cerebro-spinal fluid, tends to cause symptoms of acidosis and increased neuro-muscular irritability, i.e., tremors, twitchings and increased tendon jerks. The grave nervous

symptoms of uræmia such as weakness, apathy, drowsiness and coma are caused either by the increasing concentration in the blood and cerebro-spinal fluid of the non-protein nitrogenous constituents, or by the retention of the phenol derivatives, the normal limit of which is 1.1 to 1.4 mgm. per cent. These symptoms may in some cases be further evoked by the accumulation of guanidine which not only produces apathy, tremors, muscular twitchings and convulsions but also stupor and coma. The respiratory symptoms of increased pulmonary ventilation and periodic breathing are due to diminution of the alkaline reserve of the blood owing to an increase in the inorganic phosphates. The gastro-intestinal symptoms, particularly nausea and vomiting as well as diarrhœa and colitis, may be caused by the accumulation of guanidine and also by the irritating effects of toxic substances during their excretion through the mucous membrane of the alimentary tract. The hæmorrhagic symptoms which are sometimes seen either as petechial hæmorrhages or as severe uncontrollable bleeding from the gums, may be explained on the basis of the increased capillary permeability brought about by the intoxication as well as by the hypocalcæmic condition of the blood. Last of all, the emaciation and anæmia in advanced cases are due to the low food intake and deficient absorptive power of the intestines. Thus almost all the important symptoms of uræmia are explained on the chemical basis, although we are not yet able to solve the primary problem which initiates such chemical changes.

There is one important point which may be discussed in connection with uræmia, and this is the nature of the renal function when the acid-base equilibrium of the blood and tissues becomes considerably altered. The commonest example is the upset of the kidney function when ketosis and coma develop in the course of diabetes mellitus. It is often found that in cases of severe diabetic coma, in addition to the biochemical alterations characteristic of the disease, it is not at all uncommon to find blood urea as high as 100 mgm. per cent which suggests a uræmic condition superimposed as a terminal event. As the condition of coma improves the urea retention diminishes *pari passu*. Thus it may be concluded that a sudden or considerable alteration in the reaction of the blood and tissue fluids may act injuriously on the function of the kidney, producing a severe degree of renal failure. And if the organ has already been the seat of disease, the reaction becomes very violent and the uræmic condition develops. A similar change may also be brought about in alkalosis. Oakley (1935) published an account of seven cases of alkalosis occurring in the course of treatment of peptic ulcer two of which died in coma with blood urea figures of 225 and 250 mgm. per cent respectively. Intensive treatment of urinary infections by ammonium chloride and mandelic acid

may produce a marked rise in blood urea. In case of a pre-existing damage of the kidneys, this might lead to a severe degree of renal failure. It is well therefore to remember that although healthy kidneys may function well, within wide variations of the acid-base balance, damaged organs can do so only within much narrower limits. It is most important in such cases to take necessary measures to maintain the alkali reserve at as normal a level as possible.

#### *Clinical picture*

It is essential to remember that if renal failure is gradual, the nitrogen retention will also be slow and insidious in its increase and it may reach an extreme degree before any clinical disturbance is produced. On the other hand, if the change comes on suddenly, the symptoms make their appearance acutely before any considerable accumulation of urea and non-protein nitrogen has taken place. An appreciation of these facts will explain the occurrence of a classical uræmic syndrome without any marked biochemical alteration in the blood and tissue fluids. Typical examples of such a condition may be found in cases of chronic prostatic obstruction when a patient may not show symptoms of uræmia in spite of a marked chemical change in the blood.

The clinical picture has been studied in 44 cases of uræmia treated in the Medical College Hospital during the last 4 years.

because we have recently found some extreme examples of urea retention with uræmic syndrome in patients suffering from leptospiral infection. Whether this infection produces a true nephritis or not could not be actually verified by autopsy examination but clinical and biochemical findings all go to prove that it does cause such damage.

*Onset.*—The onset of uræmia is often insidious. In our series, 42 cases had a gradual onset and in only 2 was the condition ushered in with sudden convulsive seizures. Such a sudden onset is nowadays attributed to the development of vascular spasm leading to cerebral ischæmia, œdema of the brain either local or general and increased cerebro-spinal fluid tension, a group of morbid processes which are included in the term hypertensive encephalopathy (Fishberg, 1931). There is however a certain group of cases, though their number may be small, which occur particularly in young subjects and where unmistakable signs of serious kidney damage with marked urea retention may be found. There is also vascular change with marked hypertension. These are only examples of uræmia from sudden renal failure with an associated hypertensive encephalopathy as a complication (case 38).

*General appearance.*—Many of the patients had a peculiar sallow waxy appearance, very marked in some cases. In long-standing cases, emaciation was quite obvious. In this series

TABLE I  
*Age incidence*

Age in years	Nephritis	Nephrosclerosis with hypertension	Weil's disease	Nephrosclerosis without hypertension	Enlarged prostate	Cystitis	Extra renal cause	Unknown	Total
11-20	5	..	..	..	..	..	..	..	5
21-30	4	..	1	..	..	1	1	..	7
31-40	4	..	4	..	..	..	..	1	9
41-50	4	1	..	1	..	..	..	..	6
51-60	1	5	..	1	..	..	..	..	7
61-70	..	5	..	..	2	..	..	..	7
71-80	..	..	..	2	1	..	..	..	3
TOTAL	18	11	5	4	3	1	1	1	44

The oldest patient was 80 and the youngest 14 years old. The largest number occurred during the sixth and seventh decades of life, but in the nephritic group of cases the patients were younger.

*Sex.*—Out of 44 cases, 42 occurred in males and only 2 in females. But hardly any conclusion can be deduced from such figures in our country where females seek hospital treatment much less than males.

*Predisposing diseases.*—A study of table I will give an idea of this subject. Nephritis and nephrosclerosis do not require any comment. Weil's disease has been included in the list

12 showed this feature and 6 of them belonged to the nephritic group.

*Nervous symptoms.*—The commonest symptom was found to be drowsiness coming on slowly and ending in coma. There were however a few cases which were boisterous, especially at night, and violent occasionally. Some patients were always found in a depressed mood, not taking the slightest interest in their surroundings and even neglecting their food. Mental confusion was noticed in some in whom there were both incoherent speech and thought. Hallucinations and a paranoiac condition may also exist. There was one patient belonging to

the nephrosclerotic group who would not sleep at night and would always soil his bed. When asked why he did so he would persistently say that he could not get the urine bottle in his bed as the latter would constantly leave him and go about in the wards. Troublesome insomnia, especially at night, is fairly common. The patient may remain up the whole night, wide awake and restless but pass the day in sleep. Contrary to the popular conception, headache is rarely complained of. Convulsive seizures were present in two cases only. Occasional twitching movements of muscles may be noted. Weakness and marked prostration were very constant, but paralysis was never met with unless there were associated cerebral vascular lesions. Some cases complained of transient dimness of vision but sudden amaurosis was infrequent, being present in 2 cases only.

*Respiratory symptoms.*—Apart from those due to supervening complications or associated diseases, bronchitis, emphysema, broncho-pneumonia, pleurisy, etc., respiratory difficulty was not common. The classical observation of Rose Bradford, namely, dyspnoea of a hissing character in a drowsy patient with bleeding gums, although very characteristic, was seen in 5 cases only. Cheyne-Stokes type of breathing was present in 3 cases.

*Gastro-intestinal symptoms.*—Constipation was present in the majority, being found in 25 cases and diarrhoea in 9 cases. A superficial glossitis with glazed and raw red tongue in an elderly patient with some drowsiness is almost diagnostic. There may be anorexia, nausea, vomiting, stomatitis and hiccough. In this series 9 patients had nausea and vomiting, 7

*Cardio-vascular symptoms.*—The symptoms referred to the cardio-vascular system are due to the primary condition which gave rise to uræmia. In the majority of instances, both in the nephritic and the nephrosclerotic groups, there were varying degrees of cardiac enlargement with or without cardiac failure. The latter condition is due to myocardial degeneration brought about by ischæmic fibrosis as a result of coronary arteriosclerosis. In some of the cases, we could find the most remarkable enlargement of the organ, the apical impulse being felt in the 7th left inter-space in the mid-axillary region. The heart rate is usually high. Gallop rhythm, cardiac arrhythmias including auricular fibrillation and apical systolic murmurs due to relative incompetence may all be found. In some of our cases, gallop rhythm was present throughout the course of the illness.

Involvement of the pericardium as a terminal infection is not infrequent, being present in 2 of our cases. It may be dry pericarditis or one with effusion, the former being the commoner of the two. It is usually ushered in by a rise of temperature which cannot be explained. There is hardly any complaint of pain as the patient remains more or less in a semi-comatose condition. Precordial pain may however be complained of if there is coronary arterial involvement. In the present series 3 such cases were found, the diagnosis being established by electrocardiographic examination. An attack of coronary thrombosis may be the cause of sudden death in uræmia (case 14). There are usually marked arterial changes in all cases due to nephritis and nephrosclerosis.

TABLE II  
Blood pressure in mm. of mercury

Predisposing diseases	SYSTOLIC			DIASTOLIC		
	Highest	Lowest	Mean	Highest	Lowest	Mean
Nephritis	220	95	175	140	65	110
Nephrosclerosis with hypertension	265	140	196	190	120	117

hiccough and 3 bleeding gums one of which was very severe and uncontrollable and ended fatally. Two cases apparently suffering from colitis could be followed up and on autopsy examination one showed generalized congestion of the colon with small superficial ulcers and the other had hæmorrhages in the submucous layer.

*Hæmorrhages.*—Petechial hæmorrhages in the skin were found in 2 cases. Petechial hæmorrhage and ecchymoses were present in 2 cases. Only 1 case had frank hæmaturia. Mention has already been made about bleeding from mucous surfaces, especially from the gums. As a rule, the loss of blood is never pronounced but Konar (1939) reported a case in which it was so severe and uncontrollable that the patient died of exsanguination. Gross blood in the stool is uncommon.

Highest pressure recorded was in case 39 who had nephrosclerosis with hypertension S/D = 265/190. No remarkable change in blood pressure was noticed in cases of Weil's disease. This high blood pressure usually comes down with the onset of cardiac failure. A falling blood pressure in a drowsy patient who had previously suffered from hypertension is always ominous.

*Temperature.*—Uncomplicated cases of uræmia do not show any rise of temperature. If it is present, one should suspect the onset of some complication such as pericarditis, broncho-pneumonia or infection in the urinary tract. Case 38 which was admitted with convulsions ran a temperature varying from 101° to 103°F. This patient succumbed within 12 hours of admission. As a rule, the temperature

is low, varying from 99° to 101°F. The Weil's disease group of cases, did not show any rise of temperature as they were usually admitted after the 7th day of illness when the disease had become apyrexial.

*Blood changes.*—Anæmia of a hypochromic microcytic type is common especially in the nephritic group of cases. Moderate degree of leucocytosis with polymorphonuclear preponderance is common.

with albumin and casts, and a rise of blood urea and N. P. N. above 100 mgm. per cent. On the other hand, the acute convulsive uræmia is characterized by the sudden onset, presence of severe headache, epileptiform convulsions, paralysis, transient palsies, amaurosis, maniacal delirium, cardio-vascular changes, hypertension, neuro-retinopathy, scanty urine of a high specific gravity and a normal blood chemistry or a slight increase of blood urea and N. P. N. It

TABLE III  
*Biochemical changes*

Predisposing diseases	UREA			N. P. N.		
	Highest	Lowest	Mean	Highest	Lowest	Mean
Nephritis .. .. .	281	37	102	120	39	75
Nephrosclerosis with hypertension ..	224	35	89	206	34	75
Weil's disease .. .. .	410	115	244	245	84	168
Nephrosclerosis without hypertension	140	30	74	70	32	58

In some of the cases in our series, the amount of urea and non-protein nitrogen remained within normal limits, but this was due to the fact that either the blood was collected when uræmia did not actually set in or when the patient recovered from the condition with treatment.

*Urine.*—In all our cases the quantity of urine was markedly diminished and reached as low as 4 ounces in 24 hours. Uræmia may, however, occur while the patient has been passing a large quantity of urine. But in such cases, it is very pale, almost watery and contains little or no solid and pigmentary constituents. The lowest specific gravity that was noted in the series was 1.002. Albumin was present in all the cases, being marked in the nephritic group. It was as high as 0.8 per cent in case 30. Tube casts were detected in 30 cases—hyaline and granular in 27, only hyaline in 3. They were more frequently present in the nephritic than in any other group. Although frank hæmaturia was present in one case only, red blood cells were found in the centrifugized deposit in 17 cases, of which 11 were nephritic. It is a point of interest that red cells persist in the urine most tenaciously and would not disappear under any treatment.

*Diagnosis.*—In practice the diagnosis of true retention uræmia from the acute convulsive type is essential from the point of view of prognosis and treatment. The diagnostic features of true retention uræmia are the insidious onset, the emaciated and anæmic facies, muscular weakness, apathy, drowsiness gradually passing into stupor and coma, nocturnal insomnia with boisterousness, muscular twitchings, brisk reflexes, ammoniacal odour of the breath, stomatitis with bleeding gums, anorexia, vomiting and diarrhœa, respiration deep and slow, or of the hissing type, scanty urine of a low specific gravity

must be remembered, however, that both conditions may co-exist.

*Prognosis.*—The ultimate outlook is influenced by the underlying cause and the possibility of its removal. In retention uræmia of chronic nephritis, the prognosis is obviously bad because it is the end result of a high grade renal failure. In most cases the fatal outcome is a question of a few days or a few weeks, depending on the degree of coma, the presence of periodic or air-hunger type of breathing, stomatitis with bleeding gums, purpuric manifestations, persistent hiccough, pericarditis and a falling temperature, associated with a blood urea or N. P. N. of over 150 mgm. per cent and creatinine over 5 mgm. Creatinine figures above 12 mgm. indicate death within three weeks. Nephritic cases which may show temporary improvement often relapse and very few of them survive a year. In our experience only 2 of our cases did survive for a year. Cases of retention uræmia due to chronic urinary obstruction by enlarged prostate have a better outlook if the cause is removed. Similarly the prognosis of uræmia in diabetic ketosis, acidosis and alkalosis is favourable because the acid-base disturbance may be successfully tackled. The prognosis of acute convulsive uræmia on the other hand is favourable, unless recurrent attacks of convulsions bring about a cardiac failure. In acute nephritis and eclampsia gravidarum the patient may, by proper management, frequently be tided over the so-called uræmic stage to a stage of recovery.

The end results of uræmia are evident from table IV.

*Treatment.*—The main principles of treatment in cases of uræmia consist of—(a) removal of the underlying cause if possible, (b) correction of the altered blood chemistry

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
1	80	M.	Onset gradual	Drowsiness	<i>Nil</i>	Diarrhœa, colitis (fair number of pus cells in stool).	Breathlessness, palpitation. B. P.—150/90.	None seen.
2	72	M.	Do.	Weakness, prostration, drowsiness, headache.	<i>Nil</i>	Hiccough, nausea, diarrhœa (fair number of pus cells in stool).	B. P.—130/104.	<i>Nil</i>
3	62	M.	Do.	Drowsiness	<i>Nil</i>	Diarrhœa	B. P.—115/75	<i>Nil</i>
4	42	M.	Do.	No drowsiness. Conscious.	<i>Nil</i>	Nausea, vomiting.	Breathlessness. Precordial pain. B. P.—220/130.	<i>Nil</i>
5	40	M.	<i>Nil</i>	Unconsciousness, epileptiform convulsions.	<i>Nil</i>	<i>Nil</i>	B. P.—220/110	<i>Nil</i>
6	27	M.	Onset gradual. Emaciation—marked.	Drowsiness	<i>Nil</i>	Bilious vomiting and diarrhœa.	Pericardial rub, gallop rhythm. B. P.—170/130.	Neuro-retinopathy.
7	69	M.	Onset gradual	Do.	<i>Nil</i>	Constipation	Breathlessness, palpitation. B. P.—170/80.	<i>Nil</i>



BLE

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Sp. gr.—1012. Albumin—present in fair amount. Hyaline and granular casts. Fair number of pus cells.	101°F.	Urea—50 mgm. %.	Hæmoglobin—75%. Total leucocyte count—12,187 per c.mm. Polymorphonuclear neutrophils—80%. Lymphocytes—18%. Monocytes—2%.	Cardiac failure. Enlarged prostate. Cystitis.	Death.
Sp. gr.—1012. Albumin—marked. Plenty of granular and hyaline casts.	Normal	Urea—140 mgm. %. N. P. N.—100 mgm. %.	Hæmoglobin—70%. Total leucocyte count—16,848 per c.mm. Polymorphonuclear neutrophils—82%. Lymphocytes—16%. Monocytes—2%.	Nephrosclerosis without hypertension.	Cured (urea on discharge 24 mgm. %).
Sp. gr.—1008. Albumin—marked, plenty of pus cells. Tube casts— <i>nil</i> .	101°–103°F.	Urea—120 mgm. %. N. P. N.—82 mgm. %.	Hæmoglobin—60%. Total leucocyte count—15,125 per c.mm. Polymorphonuclear neutrophils—80%. Lymphocytes—18%. Monocytes—2%. Polymorphonuclear eosinophils— <i>nil</i> .	Enlarged prostate. Cystitis.	Death.
Sp. gr.—1002. Albumin—marked. A few granular casts. Fair number of pus cells.	Normal	Urea—140 mgm. %. N. P. N.—101 mgm. %.	Hæmoglobin—45%. Total leucocyte count—13,416 per c.mm. Polymorphonuclear neutrophils—78%. Lymphocytes—20%. Monocytes—2%.	Chronic nephritis. Hypertension, congestive cardiac failure.	Do.
Sp. gr.—1012. Tube casts, hyaline casts and granular casts.	Do.	Urea—98 mgm. %. N. P. N.—68 mgm. %.	Hæmoglobin—60%. Total leucocyte count—32,760 per c.mm. Polymorphonuclear neutrophils—85%. Lymphocytes—15%.	Unknown.	Do.
Sp. gr.—1004. Albumin—moderate. Pus cells—fair number. R. B. C.—a few. Casts—not found.	Do.	Urea—120 to 281 mgm. %. N. P. N.—94 to 98 mgm. %.	Hæmoglobin—50%. Total leucocyte count—6,400 per c.mm. Polymorphonuclear neutrophils—62%. Lymphocytes—34%. Monocytes—2%. Polymorphonuclear eosinophils—2%.	Chronic nephritis. Cardiac failure.	Do.
Sp. gr.—1024. Albumin—fair amount. Pus cells—a few. Hyaline casts—a few.	Do.	Urea—40 mgm. %. N. P. N.—34 mgm. %.	Hæmoglobin—75%. Total leucocyte count—6,524 per c.mm. Polymorphonuclear neutrophils—68%. Lymphocytes—26%. Monocytes—2%. Polymorphonuclear eosinophils—4%.	Nephrosclerosis with hypertension. Hypertensive cardio-renal failure.	Cured. Later died of uræmia. Broncho-pneumonia (1 year later).

TABLE

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
8	65	M.	Onset gradual	Insomnia	<i>Nil</i>	Constipation	Breathlessness, palpitation. B. P.—165/100.	<i>Nil</i>
9	45	M.	Sudden	Convulsions, unconscious.	<i>Nil</i>	Do.	B. P.—134/96	<i>Nil</i>
10	28	M.	Onset gradual. Petechial spots all over the body.	Drowsiness	<i>Nil</i>	Bleeding from the gums for 3 days. Marked jaundice.	B. P.—140/110	<i>Nil</i>
11	18	M.	Onset gradual. Emaciation—moderate.	Do.	Blood stained frothy sputum.	Constipation	Breathlessness, palpitation. B. P.—165/120.	<i>Nil</i>
12	56	F.	Onset gradual	Drowsiness and coma.	<i>Nil</i>	Do.	Pericarditis. B. P.—184/120.	<i>Nil</i>
13	65	M.	Do.	Unconscious. Marked weakness.	<i>Nil</i>	Do.	B. P.—210/150	<i>Nil</i>
14	16	F.	Onset gradual. Slight emaciation.	Drowsiness	<i>Nil</i>	Do.	Dyspnoea. Pericarditis. B. P.—180/20.	<i>Nil</i>

—contd.

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Sp. gr.—1028. Albumin—fair amount. Sugar—trace. Pus cells—a few.	Normal	Urea—60 mgm. %. N. P. N.—56 mgm. %.	Hæmoglobin—60%. Total leucocyte count—6,552 per c.mm. Polymorphonuclear neutrophils—64%. Lymphocytes—32%. Monocytes—2%. Polymorphonuclear eosinophils—2%.	Nephrosclerosis with hypertension. Hypertensive cardio-renal failure. Diabetes mellitus.	Cured. Died 6 months later of renal failure.
Sp. gr.—1020. Albumin—fair amount. Hyaline and granular casts—in fair number. Pus cells—a few. Epithelial cells—a few.	101.6°F.	Urea—82 mgm. %. N. P. N.—70 mgm. %.	Hæmoglobin—70%. Total leucocyte count—8,112 per c.mm. Polymorphonuclear neutrophils—78%. Lymphocytes—20%. Monocytes—2%.	Chronic nephritis (uræmic convulsion).	Cured.
Sp. gr.—1010. Albumin—fair amount. Hyaline casts—a few. Granular casts—a few. Occult blood—nil. Bile pigment—present.	99°F.	Urea—410 mgm. %. N. P. N.—245 mgm. %. Cholesterol—262 mgm. %. van den Bergh—immediate direct positive. Bilirubin content—32 units.	Hæmoglobin—45%. Total leucocyte count—12,000 per c.mm. Polymorphonuclear neutrophils—90%. Lymphocytes—9%. Monocytes—1%.	Weil's disease (serum positive to agglutination).	Death.
Sp. gr.—1005. Albumin—moderate amount. Hyaline casts—a few. Pus cells—a few. R. B. C.—a few. Granular casts—nil.	101°F.	Urea—80 mgm. %. N. P. N.—70 mgm. %.	Hæmoglobin—55%. Total leucocyte count—17,712 per c.mm. Polymorphonuclear neutrophils—90%. Lymphocytes—10%.	Chronic nephrosclerosis with secondary hypertensive congestive cardiac failure.	Do.
Sp. gr.—1008. Albumin—trace. Hyaline casts—a few. Pus cells—a few. Epithelial cells—a few.	103°F.	Urea—140 mgm. %. N. P. N.—119 mgm. %.	Hæmoglobin—60%. Total leucocyte count—6,500 per c.mm. Polymorphonuclear neutrophils—82%. Lymphocytes—12%. Monocytes—4%. Polymorphonuclear eosinophils—2%.	Nephrosclerosis with hypertension.	Do.
Sp. gr.—1020. Albumin—moderate amount. Casts—hyaline and granular. Pus cells—fair number.	Normal	Urea—60 mgm. %. N. P. N.—45 mgm. %.	Hæmoglobin—75%. Total leucocyte count—17,472 per c.mm. Polymorphonuclear neutrophils—95%. Lymphocytes—5%.	Nephrosclerosis with hypertension. Bulbar paralysis.	Do.
Sp. gr.—1015. Albumin—moderate amount. R. B. C.—a few. Casts—nil.	101°F.	Urea—30 mgm. %.	Hæmoglobin—45%. Total leucocyte count—10,312 per c.mm. Polymorphonuclear neutrophils—85%. Lymphocytes—13%. Monocytes—nil. Polymorphonuclear eosinophils—2%.	Chronic nephritis with hypertension. Hypertensive congestive cardiac failure.	Do.

TABLE

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
15	55	M.	Gradual onset. Moderate emaciation.	Drowsiness	Cheyne-Stokes' breathing.	<i>Nil</i>	Breathlessness. B. P.—210/130.	Albuminuric retinitis.
16	36	M.	Onset gradual	Drowsiness. Restlessness. Semi-conscious, later unconscious.	Hissing breathing.	Nausea, vomiting, diarrhoea ammoniacal odour in breath.	B. P.—180/100.	<i>Nil</i>
17	32	M.	Onset gradual. Emaciation—marked.	Drowsiness	<i>Nil</i>	Vomiting, hiccough, constipation.	..	<i>Nil</i>
18	56	M.	Onset gradual. Slight emaciation.	Irritable and boisterous especially at night.	<i>Nil</i>	Constipation	B. P.—225/125	<i>Nil</i>
19	46	M.	Onset gradual. Emaciation—marked.	Drowsiness, coma.	<i>Nil</i>	Do.	B. P.—215/160	<i>Nil</i>
20	70	M.	Onset gradual	Drowsiness. Light-headed at night.	..	Diarrhoea	B. P.—175/95	
21	40	M.	Do.	Drowsiness	Dyspnoea	Constipation	B. P.—170/100	<i>Nil</i>
22	30	M.	Do.	Do.	Dyspnoea, asthmatic, inspiratory and expiratory hissing.	Do.	B. P.—185/95	<i>Nil</i>

—contd.

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Sp. gr.—1006. Albumin—moderate amount. Granular casts—a few. R.B.C.—fair number.	Normal	Urea—224 mgm. %. N. P. N.—206 mgm. %.	Hæmoglobin—45%. Total leucocyte count—12,000 per c.mm. Polymorphonuclear neutrophils—82%. Lymphocytes—16%. Monocytes—2%.	Nephrosclerosis with malignant hypertension. Congestive cardiac failure.	Death.
Sp. gr.—1012. Albumin—marked amount. Granular casts—a few. Hyaline casts—a few.	100°F.	Not done	Hæmoglobin—60%. Total leucocyte count—7,800 per c.mm. Polymorphonuclear neutrophils—76%. Lymphocytes—16%. Monocytes—8%.	Chronic nephritis	Do.
Sp. gr.—1012. Albumin—moderate. Granular casts—a few. Pus cells—plenty.	Normal	Urea—75 mgm. %. N. P. N.—75 mgm. %. Later Urea—35 mgm. %. N. P. N.—42 mgm. %.	Hæmoglobin—65%. Total leucocyte count—11,184 per c.mm. Polymorphonuclear neutrophils—92%. Lymphocytes—8%.	Chronic nephritis	Cured.
Sp. gr.—1020. Albumin—trace. Sugar—2.5%. Casts—nil.	Do.	Urea—135 mgm. %. N. P. N.—110 mgm. %. Sugar—0.25%.	Hæmoglobin—75%. Total leucocyte count—6,552 per c.mm. Polymorphonuclear neutrophils—78%. Lymphocytes—20%. Monocytes—1%. Polymorphonuclear eosinophils—1%.	Nephrosclerosis with hypertension. Diabetes mellitus.	Death.
Sp. gr.—1015. Albumin—moderate amount. Hyaline and granular casts.	Do.	Urea—55 mgm. %. N. P. N.—38 mgm. % (on 9-4-38).	Hæmoglobin—65%. Total leucocyte count—8,475 per c.mm. Polymorphonuclear neutrophils—72%. Lymphocytes—24%. Monocytes—2%. Polymorphonuclear eosinophils—2%.	Nephrosclerosis with hypertension. Left-sided hemiplegia. Myocardosis, coronary sclerosis.	Death 20-9-38
Sp. gr.—1010. Albumin—trace. Pus cells—fair number.	Do.	Urea—30 mgm. %. N. P. N.—23 mgm. %.	Hæmoglobin—100%. Total leucocyte count—7,812 per c.mm. Polymorphonuclear neutrophils—70%. Lymphocytes—24%. Monocytes—4%. Polymorphonuclear eosinophils—2%.	Stricture urethra. Cystitis. Enlarged prostate.	Death.
Sp. gr.—1006. Albumin—moderate amount. Pus cells—a few. R.B.C.—a few. Hyaline and granular casts—a few.	Do.	Urea—145 mgm. %. N. P. N.—120 mgm. %.	Hæmoglobin—50%. Total leucocyte count—20,000 per c.mm. Polymorphonuclear neutrophils—90%. Lymphocytes—10%.	Hypertensive congestive cardiac failure. Pleural effusion (left). Chronic nephritis.	Do.
Sp. gr.—1010. Albumin—moderate. Pus cells—plenty. R. B. C. and casts—nil.	Do.	..	Hæmoglobin—45%. Total leucocyte count—16,000 per c.mm. Polymorphonuclear neutrophils—80%. Lymphocytes—20%.	Cystitis with ascending infection of the urinary tract.	Do.

TABLE

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
23	64	M.	Onset gradual. Emaciation—moderate.	Boisterous, later drowsy.	Asthma for 20 years. Dyspnoea. Cheyne-Stokes' breathing.	Constipation	B. P.—190/130	Nil
24	40	M.	Onset gradual	Drowsiness	..	Hiccough. Constipation.	B. P.—100/60	Nil
25	58	M.	Onset gradual. Slight emaciation.	Boisterous, later drowsy.	Nil	Hiccough. Constipation.	Pain precordium. Gallop rhythm. B. P.—95/65.	Nil
26	72	M.	Onset gradual	Drowsiness	Nil	Constipation	Pain precordium. B. P.—100/65.	Nil
27	40	M.	Onset gradual. Anasarca.	Do.	Cheyne-Stokes' breathing.	Do.	B. P.—205/100	Nil
28	26	M.	Onset gradual. Generalized oedema. At the end, was markedly emaciated.	Headache. Dimness of vision since 4 months before admission. Drowsiness. Coma. Left-sided facial paralysis.	Nil	Anorexia. Spongy gums, bleeding from the gums. Throat congested. Slight fluid in abdomen.	Apex—left 6th interspace $\frac{1}{2}$ inch outside mid-clavicular line. Arterial wall—thickened. B. P.—210/130.	Tortuous arteries. Distended veins, few patches of fresh hæmorrhage.



—contd.

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Sp. gr.—1010. Hyaline and granular casts— <i>nil</i> . Albumin—trace.	101° F. on the day of death.	Urea—71 mgm. %. N. P. N.—70 mgm. %.	Hæmoglobin—55%. Total leucocyte count—7,800 per c.mm. Polymorphonuclear neutrophils—86%. Lymphocytes—10%. Monocytes—3%. Polymorphonuclear eosinophils—1%.	Nephrosclerosis with hypertension. Chronic bronchitis. Emphysema. Bronchial asthma. Hypertensive cardiac failure.	Death.
Sp. gr.—1016. Albumin—moderate. Hyaline and granular casts. Bile pigment—present. Bile salts—present.	Normal	Urea—150 mgm. %. N. P. N.—120 mgm. %. van den Bergh—immediate direct, strongly positive. Bilirubin content—45 units.	Hæmoglobin—50%. Total leucocyte count—15,620 per c.mm. Polymorphonuclear neutrophils—88%. Lymphocytes—12%.	Weil's disease	Do.
Sp. gr.—1008. Albumin—trace. Hyaline and granular casts—few.	Do.	Urea—77 mgm. %. N. P. N.—70 mgm. %. Sugar—0.14% (fasting).	Hæmoglobin—70%. Total leucocyte count—18,720 per c.mm. Polymorphonuclear neutrophils—96%. Lymphocytes—3%. Monocytes—1%.	Nephrosclerosis without hypertension. Diabetes mellitus. Coronary thrombosis.	Improved.
Sp. gr.—1020. Albumin—trace. Casts— <i>nil</i> .	Do.	Urea—30 mgm. %. N. P. N.—32 mgm. %.	Hæmoglobin—90%. Total leucocyte count—10,920 per c.mm. Polymorphonuclear neutrophils—69%. Lymphocytes—21%. Monocytes—6%. Polymorphonuclear eosinophils—4%.	Nephrosclerosis without hypertension. Bundle-branch block.	Do.
..	Do.	Urea—185 mgm. %. N. P. N.—162 mgm. %.	Hæmoglobin—50%. Total leucocyte count—12,480 per c.mm. Polymorphonuclear neutrophils—78%. Lymphocytes—20%. Monocytes—1%. Polymorphonuclear eosinophils—1%.	Chronic nephritis	Death.
Sp. gr.—1012. Albumin—0.3%. Occult blood—present. Few pus cells. Few epithelial cells. Fair number of R. B. C. Casts— <i>nil</i> .	Do.	22-2-39. Urea—63 mgm. %. N. P. N.—45 mgm. %. Cholesterol—332 mgm. %. Chloride—468 mgm. %. Ca—10 mgm. %. 24-2-39. Urea—80 mgm. %. N. P. N.—60 mgm. %.	22-2-39. Hæmoglobin—60%. Total erythrocyte count—3,500,000 per c.mm. Total leucocyte count—12,500 per c.mm. Polymorphonuclear neutrophils—80%. Lymphocytes—18%. Monocytes—2%. 1-3-39. Hæmoglobin—40%. R. B. C.—2,250,000 per c.mm. W. B. C.—11,820%. Polymorphonuclear neutrophils—78%. Lymphocytes—20%. Monocytes—2%.	Chronic nephritis with secondary hypertension.	Death 1-3-39.

TABLE

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
29	60	M.	Onset gradual. Slight emaciation.	Boisterousness in between. Drowsy, coma.	Evidence of chronic bronchitis with emphysema.	Vague symptoms of dyspepsia for the last 3 years before admission.	Palpitation, arteries markedly thickened. B. P. on admission, 165/105, 1 month later 195/130. E. C. G.—myocardial degeneration and coronary sclerosis.	Nil
30	51	M.	Onset gradual. Admitted with the complaints: 1. Generalized swelling of the body 10 days after an exposure to chill. 2. Scanty micturition. 3. Abdominal pain.	Drowsiness	Evidence of bilateral broncho-pneumonia.	Constipation	B. P.—180/100 on admission. Gradually came down to 118/80 on the day of death. Arteries thickened.	Nil.
31	29	M.	Onset gradual. Markedly pale.	Cramps and tingling sensation of the extremities. Sense of weakness and exhaustion. Later extreme languor, drowsiness and coma. Dimness of vision.	Nil	Nausea, vomiting, constipation.	Palpitation. Arteries thickened and tortuous. Heart irregular at the end. B. P.—210/115.	Flame-shaped old hæmorrhage in both eyes, more marked in the right.
32	45	M.	Onset gradual. Pale and waxy in appearance. Marked emaciation.	Headache. Insomnia. Extreme languor. Marked exhaustion and drowsiness.	Nil	Hiccough, nausea, vomiting, diarrhoea, fair number of pus cells in stool.	Arteries thickened. B. P.—134/80 which gradually came down to 82/54.	Nil

—contd.

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Sp. gr.—1004. Albumin—present. Hyaline and granular casts—few.	Normal	On admission— Urea—38 mgm. %. N. P. N.—40 mgm. %. Cholesterol—152 mgm. %. Chloride—410 mgm. %. 11-4-39. Urea—74 mgm. %. N. P. N.—70 mgm. %. Cholesterol—285 mgm. %. Chloride—430 mgm. %.	Hæmoglobin—50%. Total erythrocyte count—2,850,000 per c.mm. Total leucocyte count—7,312 per c.mm. Polymorphonuclear neutrophils—88%. Lymphocytes—8%. Monocytes—4%.	Chronic bronchitis with emphysema. Hypertensive cardiac failure. Nephrosclerosis. Post-mortem findings: Generalized arteriosclerosis. Cardiac dilatation and hypertrophy. Arteriosclerotic kidney. Œdema lungs. Hæmorrhages within large gut. Œdema brain.	Death 11-4-39.
Hæmaturia. Sp. gr.—1022. Albumin—0.8%. R. B. C.—plenty. Tube casts—hyaline and granular.	Remittent temperature for 7 days after admission. Maximum —102°F. Minimum —99°F.	20-5-39. Urea—65 mgm. %. N. P. N.—45 mgm. %. Chloride—410 mgm. %. Cholesterol—140 mgm. %. Creatinine—3 mgm. %. 25-5-39. Urea—68 mgm. %. N. P. N.—63 mgm. %.	Hæmoglobin—90%. Total erythrocyte count—4,610,000 per c.mm. Total leucocyte count—13,728 per c.mm. Polymorphonuclear neutrophils—80%. Lymphocytes—8%. Monocytes—2%. Polymorphonuclear eosinophils—10%.	Chronic nephritis. Broncho-pneumonia.	Death 3-6-39.
Quantity—about 40 oz. on admission, which gradually came down to 15 to 20 oz. Sp. gr.—1010. Albumin—0.12%. Pus cells, R. B. C.—a few. Fair numbers of hyaline and granular casts.	Normal	Urea—170 mgm. %. N. P. N.—120 mgm. %. Cholesterol—260 mgm. %. Chloride—351 mgm. %.	Hæmoglobin—50%. Total erythrocyte count—3,230,000 per c.mm. Total leucocyte count—4,992 per c.mm. Polymorphonuclear neutrophils—60%. Lymphocytes—20%. Monocytes—18%. Polymorphonuclear eosinophils—2%. Basophils—2%. 29-3-39. Hæmoglobin—45%. W. B. C.—10,625. Polymorphonuclear neutrophils—76%. Lymphocytes—22%. Eosinophils—2%.	Chronic nephritis with secondary hypertension.	Death 5-7-39.
Quantity varied from 5 to 22 oz. Sp. gr.—1010. Albumin—0.1%. Few R. B. C. and pus cells. Fair number of hyaline and granular casts.	Intermittent temperature. Maximum —102°F. Minimum —97°F.	Urea—37 mgm. %. N. P. N.—39 mgm. %. Chloride—468 mgm. %.	Hæmoglobin—55%. Total erythrocyte count—2,900,000 per c.mm. Total leucocyte count—6,864 per c.mm. Polymorphonuclear neutrophils—82%. Lymphocytes—10%. Monocytes—2%. Polymorphonuclear eosinophils—6%.	Chronic nephritis	Death 25-9-39.

TABLE

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
33	27	M.	Onset gradual	<i>Nil</i>	<i>Nil</i>	Hiccough, vomiting, constipation, dry and coated tongue.	B. P.—100/68.	<i>Nil</i>
34	59	M.	Do.	Drowsiness with occasional fits of violence. Coma.	<i>Nil</i>	<i>Nil</i>	Pain p <sub>re</sub> cordium. B. P.—220/90 which gradually came down to 170/60. Arteries markedly thickened.	<i>Nil</i>
35	50	M.	Onset gradual. Admitted in a drowsy condition (patient a chronic alcoholic).	Drowsiness, involuntary passage of urine and faeces in linen.	<i>Nil</i>	Constipation	B. P.—160/85	<i>Nil</i>
36	14	M.	Onset gradual, general anasarca, which on treatment improved; but again developed oedema and then uræmia.	Drowsiness, gradually merging into coma.	Dyspnoea, hissing type of breathing (rate—52 p.m.). Oedema lungs.	Do.	B. P.—110/90	<i>Nil</i>
37	19	F.	Onset gradual, confined 1½ months before admission, massive pleural effusion on left side. On 26-1-40 developed purpuric spots over the upper and lower extremities, some of which were fairly big. In some of them bulla formation occurred. Emaciation—moderate.	Drowsiness. Towards the end coma supervened.	Dyspnoea, hissing type of breathing at the last stage (rate—30 p.m.).	<i>Nil</i>	<i>Nil</i>	<i>Nil</i>

—contd.

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Quantity 20 to 25 oz. at first, which improve up to 40 to 45 oz. Sp. gr.—1020. Albumin—trace. Few pus cells and R. B. C. Hyaline and granular casts.	Normal except a slight rise for the first 3 days.	..	Hæmoglobin—60%. Total erythrocyte count—4,100,000 per c.mm. Total leucocyte count—24,648 per c.mm. Polymorphonuclear neutrophils—94%. Lymphocytes—4%. Monocytes—2%.	Duodenal ulcer (as shown by skiagraphic evidence).	Cured, discharged on 23-8-39.
Quantity—10 to 20 oz. Sp. gr.—1015. Albumin—present. No tube casts.	Normal	18-8-39. Urea—53 mgm. %. On admission had urea content of 35 mgm. %.	Hæmoglobin—65%. Total erythrocyte count—3,600,000 per c.mm. Total leucocyte count—7,488 per c.mm. Polymorphonuclear neutrophils—69%. Lymphocytes—22%. Monocytes—1%. Polymorphonuclear eosinophils—8%.	Nephrosclerosis with hypertension. Spleen palpable.	Death 26-8-39.
Albumin—present. No R. B. C. Few pus cells. Few hyaline and granular casts.	Do.	Urea—65 mgm. %. N. P. N.—48 mgm. %.	Hæmoglobin—70%. Total erythrocyte count—4,250,000 per c.mm. Total leucocyte count—7,812 per c.mm. Polymorphonuclear neutrophils—68%. Lymphocytes—23%. Monocytes—6%. Polymorphonuclear eosinophils—3%.	Nephrosclerosis	Abandoned 22-9-39.
Quantity on admission—about 10 oz. which increased up to 40 oz. with treatment but it again diminished towards the later stage. Sp. gr.—1004. Albumin—0.36%. R. B. C.—few. Pus cells—fair numbers. Fair numbers of hyaline and granular casts.	Normal except for a intermittent fever for 3 to 4 days.	Total Protein—0.05%. Albumin—0.04%.	Hæmoglobin—55%. Total erythrocyte count—3,100,000 per c.mm. Total leucocyte count—5,616 per c.mm. Polymorphonuclear neutrophils—70%. Lymphocytes—28%. Monocytes—2%.	Subacute nephritis.	Death 18-10-39.
Quantity—15 oz. on admission, which improved up to about 25 oz. on treatment. But it again diminished towards the end (5 to 6 oz.). Albumin + +. No R. B. C. Fair number of pus cells. Fair number of hyaline and granular casts.	Normal except for a intermittent for 6 to 7 days.	Blood chemistry could not be investigated as wherever needle was put in hæmorrhages occurred. Coagulation time—12 minutes. Bleeding time—2 minutes 45 seconds. Hæmolysis started at 0.44% of saline complete at 0.38%. Size of R. B. C.—7.4 $\mu$ .	Hæmoglobin—55%. Total erythrocyte count—3,000,000 per c.mm. Total leucocyte count—10,937 per c.mm. Polymorphonuclear neutrophils—74%. Lymphocytes—22%. Monocytes—2%. Polymorphonuclear eosinophils—2%. Platelet count—50,000 per c.mm. Reticulocytes—2.1%.	Pregnancy kidney. Pleurisy with effusion. Parotitis.	Death 8-2-40.

TABLE

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
38	16	M.	Onset sudden, admitted with convulsion (for the last 18 hours). Neck—rigid. Kernig's sign +. Lumbar puncture—clear fluid under slight pressure.	Clonic convulsions every 2 to 3 hours. In between attacks patient comatose. Deep reflexes—exaggerated. Plantar reflex—extensor. Abdominal reflex—lost.	Nil	Nil	B. P.—190/140	Nil
39	55	M.	Onset gradual. Patient had bleeding gums.	Coma	Nil	Nil	Apex—6th left space, anterior axillary line. B. P.—265/190.	Nil
40	35	M.	Gradual onset. Toxic jaundice—very intense. Admitted on 13th day of illness.	Drowsiness ending in coma.	Dyspnoea, breathing being of hissing type (rate—30 p.m.).	Dry and coated tongue. Diarrhoea (few pus cells and R. B. C. in stool).	B. P.—170/80	Nil
41	50	M.	Onset gradual. Marked pallor. He also had swelling of the face, legs and ascites. Petechial spots over the chest; later developed ecchymoses on both forearms.	Do.	Evidence of pleural effusion left.	Constipation	B. P.—135/75. Evidence of pericardial effusion, palpitation.	Nil



—contd.

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Albumin—marked. Plenty of R. B. C. Few pus cells. Plenty of granular casts. Fair number of hyaline casts.	Continuous temperature (101° to 103°F.).	Urea—52 mgm. %. N. P. N.—46 mgm. %. Cholesterol—133 mgm. %. Chloride—468 mgm. %.	Hæmoglobin—70%. Total leucocyte count—18,750 per c.mm. Polymorphonuclear neutrophils—88%. Lymphocytes—10%. Monocytes—2%.	Acute nephritis(?)	Death (at 11-20 p.m.) on the day of admission.
.	Normal	Urea—60 mgm. %. N. P. N.—53 mgm. %. Cholesterol—140 mgm. %. Chloride—386 mgm. %.		Nephrosclerosis with hypertension.	Death 3-3-40.
Quantity—about 30 oz. at the beginning which gradually diminished to about 10 oz. at the last stage. Sp. gr.—1012. Albumin—0.8%. Bile salts and pig.—present. Pus cells and R. B. C.—a few. Granular and hyaline casts.	Do.	Urea—265 mgm. %. N. P. N.—234 mgm. %. Cholesterol—204 mgm. %. Chloride—403 mgm. %. Ca—8.1 mgm. %. van den Bergh—immediate direct positive. Bilirubin content—53 units. Coagulation time—3½ minutes. Bleeding time—3½ minutes. Hæmolysis started at 0.36%, complete at 0.26% saline.	Hæmoglobin—65%. Total leucocyte count—11,875 per c.mm. Polymorphonuclear neutrophils—84%. Lymphocytes—12%. Monocytes—4%. Platelet count—110,000 per c.mm. Reticulocytes—0.2%.	Weil's disease (agglutination positive).	Death 11-10-39.
Quantity—20 to 30 oz. Sp. gr.—1020. Albumin +. Occult blood +. Few R. B. C., few pus cells, fair number of hyaline and granular casts.	Do.	Urea—62 mgm. %. N. P. N.—52 mgm. %. Chloride—351 mgm. %. Ca—10 mgm. %. Bleeding time—7½ minutes. Coagulation time—4½ minutes. Hæmolysis commenced at 0.4% saline, complete at 0.24% saline.	Hæmoglobin—70%. Total erythrocyte count—3,850,000 per c.mm. Total leucocyte count—10,312 per c.mm. Polymorphonuclear neutrophils—75%. Lymphocytes—22%. Monocytes—2%. Polymorphonuclear eosinophils—1%. Platelet count—180,000 per c.mm. Reticulocytes—0.2%. Size of R. B. C.—7.4μ	Subacute nephritis. Pleurisy with effusion (left). Pericardial effusion.	Death 27-3-40.

TABLE

Case No.	Age	Sex	Onset and general features	Nervous symptoms	Respiratory symptoms	Gastro-intestinal symptoms	Cardio-vascular symptoms	Retinal changes
42	35	M.	Onset gradual. Admitted on 9th day of illness, jaundice + +.	<i>Nil</i>	<i>Nil</i>	Nausea, vomiting, constipation.	B. P.—108/70. Arteries—healthy.	<i>Nil</i>
43	35	M.	Onset gradual. Admitted on 4th day of illness. Jaundice + +. Fever—no fever after admission. Toxic sub-conjunctival hæmorrhage. 7-1-40 Epistaxis. 10-1-40 Hæmaturia and blood with stool.	<i>Nil</i>	<i>Nil</i>	Diarrhœa (few R. B. C. and pus cells in stool).	B. P.—135/80. Arteries—slightly thickened.	<i>Nil</i>
44	28	M.	Onset gradual. Emaciation—moderate. Pallor—very marked. Swelling of face and legs.	Drowsiness	Dyspnœa	Hiccough, constipation.	B. P.—220/140 on admission, which gradually came down to 125/70. Arteries markedly thickened. Apex—left 7th space anterior axillary line. Heart block.	<i>Nil</i>

and of the physical disturbance of the intracranial circulation and (c) relief of distressing and urgent symptoms.

TABLE IV  
*Prognosis*

Total number of cases	Immediate mortality	Remote mortality	Apparent cure	Improved	Untraced
44	33 died 75%	2 4.5%	5 11.5%	2 4.5%	2 4.5%

In view of the underlying cause being irremovable in most cases of uræmia except in those caused by mechanical obstruction to urinary outflow, our main object in every case

should be directed towards restoration of the blood chemistry to a level as near to normal as possible, and to a reduction of the raised intracranial pressure if there be any. For this purpose we must promote the elimination of toxic substances through the bowels, skin and kidneys. Rectal administration of 6 ounces of 25 per cent solution of magnesium sulphate by the drip method is a very useful means of elimination by the bowels, especially in comatose cases. It also withdraws by osmosis a large amount of fluid from the circulation and thus reduces the intracranial tension. In conscious patients, however, the hypertonic saline acts as an irritant and causes a burning sensation in the rectum which is often unbearable. In such cases we prefer the oral administration of an ounce of a saturated solution of magnesium sulphate.

—concl'd.

Urinary findings	Temperature	Blood chemistry	Blood count	Associated diseases and complications	Result
Sp. gr.—1010. Albumin—present. Bile salts and pig.—present. Fair number of pus cells. Few granular casts.	Normal except for 3 to 4 days in the 3rd week when it went up to 103°F.	23-12-39. Urea—115 mgm. %. N. P. N.—84 mgm. %. Chloride—351 mgm. %. Cholesterol—166 mgm. %. van den Bergh—immediate direct positive. Bilirubin content—20 units, 16-1-40. Urea—78 mgm. %. N. P. N.—42 mgm. %.	Hæmoglobin—75%. Total leucocyte count—8,737 per c.mm. Polymorphonuclear neutrophils—76%. Lymphocytes—20%. Monocytes—2%. Polymorphonuclear eosinophils—2%. In the third week. W. B. C.—10,625 per c.mm. Polymorphonuclear neutrophils—82%. Lymphocytes—14%. Monocytes—4%.	Weil's disease (serum positive, agglutination to classical strain).	Cured, discharged on 22-1-40.
Sp. gr.—1012. Albumin—trace. Bile salts and pig.—present. Occult blood +. Fair number of R. B. C. Fair number of pus cells. Fair number of granular casts.	Subnormal	Urea—245 mgm. %. N. P. N.—144 mgm. %. Cholesterol—180 mgm. %. Chloride—387 mgm. %. Hæmolysis started at 0.48% saline, complete at 0.24% saline.	Hæmoglobin—70%. Total leucocyte count—9,375 per c.mm. Polymorphonuclear neutrophils—86%. Lymphocytes—10%. Monocytes—2%. Polymorphonuclear eosinophils—2%. Reticulocytes—2.5%. Size of R. B. C.—7.4μ.	Weil's disease.	Death 12-1-40.
Sp. gr.—1012. Albumin—0.45%. Pus cells—plenty. Few R. B. C. Few granular casts.	Do.	Urea—135 mgm. %. N. P. N.—85 mgm. %. Cholesterol—150 mgm. %. Chloride—409 mgm. %.	Hæmoglobin—55%. Total leucocyte count—9,718 per c.mm. Polymorphonuclear neutrophils—72%. Lymphocytes—22%. Monocytes—2%. Polymorphonuclear eosinophils—4%.	Chronic nephritis with secondary hypertension, cardiac failure with heart block.	Death 2-3-40.

Elimination of toxins by the skin may be obtained by simple measures such as hot baths, hot packs, hot-air baths (radiant heat) and by the use of mild diaphoretic mixtures. Vigorous measures to promote sweating such as injections of pilocarpine nitras must be avoided in view of their depressant effect on the circulation. Elimination by the kidneys may be attempted by dilution of the blood by the administration of adequate amount of fluid orally, rectally or subcutaneously. Diuresis may be promoted by the administration of glucose, 5 per cent solution in distilled water, which is chosen for the rectal or subcutaneous route, whereas 25 to 50 per cent solution is used for the intravenous route. Intravenous administration of 25 to 50 per cent solution of cane sugar has been advocated for the same purpose. Sodium chloride is to be

avoided because it may produce oedema and oliguria. In cases associated with marked venous congestion and hypertension, withdrawal of 10 to 15 ounces of blood by venesection would reduce the toxic load and relieve the strain on the heart. The application of 6 to 8 leeches over the liver area is also useful for the same purpose. Lumbar puncture is of great value only in presence of signs of raised intracranial pressure, associated with hypertension. Apart from eliminative measures and venesection, the uræmic toxæmia may be reduced by control of the diet which should consist of a liberal amount of fluids such as plain water, barley water, fruit juice and of easily assimilable carbohydrates, e.g., glucose; the protein intake should be strictly limited to an allowance of about 0.6 gm. or even less per kilo. of the body-weight.

Our next attempt should be directed towards the relief of symptoms by appropriate remedies. The nervous symptoms such as restlessness, delirium and insomnia will improve under the administration of sedatives like bromides and chloral hydrate in addition to the eliminative measures. Severe headache and convulsive attacks are definite indications for lumbar puncture and intravenous use of hypertonic glucose solution. Morphine and barbiturate preparations such as luminal have to be used with caution in view of their defective elimination by the kidneys. The danger of their use has, however, been exaggerated. The muscular twitchings and manifestations of tetany, if any, may be controlled by the injection of 5 to 10 c.cm. of 10 per cent calcium gluconate solution. The respiratory symptoms of dyspnoea and periodic breathing may be relieved by the correction of acidosis with the administration of 2 per cent solution of sodium bicarbonate by the intravenous or the rectal route. If possible, sodium bicarbonate may be given by the mouth in doses of half to one drachm four hourly. The hæmorrhagic symptoms may be combated by the use of large doses of vitamin C parenterally and by injections of calcium salts. The results are however disappointing. Last but not least, suitable remedies must be applied for associated complications.

The writers take this opportunity to express their thanks to Colonel J. C. De, M.R.C.P. (Lond.), I.M.S., Superintendent, Medical College Hospital, for permission to use the records. They are also thankful to Dr. Amulya Ratan Roy, M.B., Dr. Ismail Ilias, M.B., and Dr. Md. Ibrahim, M.B., for their ungrudging help in collecting the case records. For the biochemical reports, they are greatly indebted to Capt. P. De, F.R.C.P. (Edin.), Professor of Physiology, Medical College, Calcutta.

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## A Mirror of Hospital Practice

### A CASE OF NEUROMYELITIS OPTICA

By S. SHONE, M.D. (Lond.), M.R.C.P. (Lond.)  
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THE following case is considered worthy of record because it presents certain unusual features, even if agreement is reached upon the suggested diagnosis, and because I am unaware of any previous mention of the disease in India.

#### Case history

Karpakam, a female Hindu child of 7 years, was admitted into the Madras General Hospital, under Liéut.-Colonel McRobert, I.M.S., on the 23rd November, 1939. The complaint was blindness and inability to use the lower limbs. There had been no previous illnesses of note, the family history was negative and the dietary habits similar to those of her class, i.e., non-vegetarian.

The child had been attending school six days before admission and had been in perfect health. She suddenly developed blindness and at the same time was unable to use both her legs. She had not been heard to speak since the onset of the illness. There had been no associated headache, fever or other bodily disturbance.

On admission, there was no pyrexia. The patient was found to be a well-nourished child and her physical

functions, as far as the limited scope of the examination demonstrated, were not grossly abnormal. It was difficult to assess whether any form of aphasia really existed, since the attitude was mainly one of negativism.

Acuity of vision was completely lost. The pupils reacted to light and were moderately dilated at rest. The discs showed no gross abnormality: there was a suggestion of blurring of the edges and some degree of hyperæmia was noted.

The other cranial nerves appeared normal.

All forms of sensation were unimpaired.

Power was normal in the upper limbs, but completely lost in the legs. There was no wasting or fibrillation.

The deep reflexes in the arms were present and equal, but the knee and ankle jerks were both absent on the two sides.

The abdominal reflexes were lost.

The visceral reflexes were unimpaired.

Both plantar reflexes were extensor.

Tonic reflexes were absent.

The spine and cranium showed no abnormality or deformity.

Examination of the other systems revealed no deviation from the normal. The urine was without abnormality. The blood picture was not in any way unusual and films showed no parasites. Blood culture was sterile and agglutinations against the typhoid group were negative. Wassermann reaction was negative. No cardiac abnormality.

The cerebro-spinal fluid was clear and under very slight pressure. Cells were 7 per c.cm., protein 30 mg.

per cent, chlorides 650 mg. per cent, sugar 100 mg. per cent, Wassermann reaction negative. Colloidal gold test negative. Culture sterile.

No treatment beyond a hexamine mixture was given. *Progress.*—

29th November. Condition unchanged as regards vision and speech. Ankle jerks normal.

2nd December. Child is able to speak and ask for things. She can just recognize the outline of objects and flinches when threatened with the hand.

12th December. Knee jerks now normal. Plantars still extensor. Now speaks normally and attempts to walk. Can definitely perceive objects but cannot apparently appreciate their colour.

22nd December. All the reflexes are normal and equal. Plantars are still 'undecided'. The child can walk, speak and see normally.

26th December. Plantar reflexes now flexor. Vision apparently quite normal, although no tests with perimeter were possible to establish the existence of any restriction of fields or of scotomata. Patient discharged and parents were admonished to bring the child again, but, so far, they have not done so.

### Discussion

Blindness of absolutely sudden onset is most unusual when occurring in a child, and blindness coupled with paraplegia is even more dramatic. The absence of any associated pyrexia or other evidence of acute inflammatory disease of the central nervous system directed the attention to the possibility of a degenerative or demyelinating lesion. The disease that first came to mind was Schilder's encephalitis, but this was ruled out by the sudden onset of symptoms and, subsequently, by the course of the malady in this case. An allied condition, disseminated sclerosis, was also considered, but this diagnosis was thought to be most improbable, both from the point of view of the age of the patient and the excessive rarity of the disease in this country. Neuromyelitis optica appeared most likely to fit the circumstances and this is the diagnosis suggested.

There are some particulars in which the present case differs from the standard description of the disease. Paraplegia is said to be due to a diffuse spinal lesion and is therefore usually associated with sensory loss and sphincter disturbance, neither of which were present in this case. We must assume that the paraplegia was the result of cortical or subcortical involvement, and that such a disturbance was also responsible for the speech defect.

Complete recovery has, it seems, rarely been recorded. It is regrettable that access to the literature on the subject is somewhat difficult under present conditions, but the disease is now described in most large textbooks and its existence as a clinical entity appears to be definitely established.

### Summary

A case of blindness, paraplegia and speech defect, occurring suddenly in a child of 7 years, is described and a complete recovery is recorded.

The diagnosis of neuromyelitis optica is suggested.

I am indebted to the Superintendent, Madras General Hospital, and to Lieut.-Colonel G. R. McRobert, I.M.S., Physician, Madras General Hospital, for their kind permission to record this case.

## A FEW CASE NOTES ON THE USE OF M. & B. 693 IN PYELITIS AND IN SEPTIC SKIN CONDITIONS\*

By R. K. DE, L.M.F., D.T.M.

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THE present-day literature is flooded with articles dealing extensively with experiments and clinical applications of M. & B. 693 in all kinds of pneumonia, in meningitis and gonorrhœa. But in such literature as is available to us, we do not find much about its use in skin diseases. We have tried it in a few cases and the result has been remarkable. And its use in 2 cases of pyelitis has also given equally satisfactory results.

### Pyelitis

*Case 1.*—Child, age 2½, was admitted into hospital on 7th August, 1939, with fever and slight bronchitis. Malaria negative. In spite of all treatment the temperature continued for 12 days. The child gradually developed toxæmia and showed signs of pyelitis. After confirming the diagnosis, the child was put on M. & B. 693 as follows:—

13th day	.. ½ tab. × 3
14th day	.. ½ tab. × 2
15th day	.. ½ tab. × 1
16th day	.. ½ tab. × 1
Total	3½ tab., i.e., 1.75 grms.

The temperature fell on 14th day and did not return. The child made uneventful recovery.

*Case 2.*—F., age 28, was admitted into hospital on 14th November, 1939, with fever for 3 days, severe toxæmia and pain over the kidney area. Malaria negative. After urine examination the case was diagnosed as one of pyelitis and was put on M. & B. 693 as follows:—

2nd day	.. 6 tab.
3rd day	.. 4 "
4th day	.. 4 "
5th day	.. 3 "
Total	17 tab., i.e., 85 grms.

The temperature came to normal on 3rd day and did not rise again. The patient made uneventful recovery.

On the 2nd and 3rd day of taking M. & B. 693, the woman vomited frequently and on two occasions she vomited round worms. Taking the vomiting as being due to round worms, M. & B. 693 was not discontinued.

### Umbilical sepsis

*Case 1.*—Child, age 13 days, was admitted into hospital on 18th November, 1939, with umbilical sepsis

\* Read at a Meeting of the Assam Frontier and Budla Beta Medical Society, held at Doom Dooma on 9th March, 1940.

and fever. In spite of all treatment at home the sepsis began to spread. The child was at once put on M. & B. 693 as follows:—

1st day	.. 1/6 tab. × 3
2nd day	.. 1/6 tab. × 2
3rd day	.. 1/6 tab. × 2

Total 1-1/6 tab., i.e., 0.6 grm. approximately.

The temperature fell on 2nd day and the umbilicus completely healed up in 6 days, when the child was discharged from hospital.

*Case 2.*—Child, age 26 days, was admitted into hospital on 6th December, 1939, with umbilical sepsis which was resistant to treatment for a long time. The sepsis was a localized one. M. & B. 693 was given as follows:—

1st day	.. 1/4 tab. × 2
2nd day	.. 1/4 tab. × 2
3rd day	.. 1/4 tab. × 2
Total	1 1/2 tab., i.e., 0.75 grm.

The umbilicus healed up and the child was discharged on 6th day.

### *Impetigo*

*Case 1.*—Child, age 1 month, was admitted into hospital on 1st May, 1939, with impetiginous sores on scalp. Local treatment for a considerable period not being satisfactory the child was put on M. & B. 693 as follows:—

1st day	.. 1/4 tab. × 3
2nd day	.. 1/4 tab. × 2
3rd day	.. 1/4 tab. × 2
4th day	.. 1/4 tab. × 2
Total	2 1/2 tab., i.e., 1.25 grms.

The sores healed up rapidly and the child was discharged on 6th day of admission.

*Case 2.*—Child, age 8 months, had impetigo on the head. In spite of local treatment at home for several days, the sores continued spreading, the neck glands got swollen and inflamed and the child was running a temperature. Pus showed staphylococci. The child was admitted into hospital on 30th June, 1939, and was put on M. & B. 693 as follows:—

1st day	.. 1/2 tab. × 2
2nd day	.. 1/2 tab. × 2
3rd day	.. 1/2 tab. × 2
4th day	.. 1/2 tab. × 2
Total	4 tab., i.e., 2 grms.

Temperature became normal after 48 hours, sores healed up rapidly, and swelling of glands also subsided fairly quickly. The child was discharged on 9th day.

*Case 3.*—Girl, age 10 years, had impetigo on face. Ordinary local treatment not being satisfactory after a few days' trial, she was admitted into hospital on 27th November, 1939, and was put on M. & B. 693 as follows:—

1st day	.. 2 tab.
2nd day	.. 1 1/2 tab.
3rd day	.. 1 1/2 tab.
4th day	.. 1 tab.
Total	6 tab., i.e., 3 grms.

All the sores healed up rapidly and she was discharged on 5th day.

### *Dermatitis*

*Case 1.*—Woman, age 40 years, was admitted into hospital on 7th June, 1939, with acute dermatitis on the whole of the dorsum of the left foot. The oozing showed staphylococci. The part was being dressed with lotio acriflavine 1 in 1,000, after cleaning with normal saline. But the infection continued spreading and she was running irregular low temperature. Hence from the 9th day she was put on M. & B. 693 as follows:—

9th day	.. 6 tab.
10th day	.. 6 tab.
11th day	.. 6 tab.
12th day	.. 3 tab.

Total 21 tab., i.e., 10.5 grms.

The temperature became normal from the 2nd day, the part healed up rapidly and she was discharged on the 20th day after admission.

She was fit for discharge on the 15th day, i.e., 7 days after beginning treatment but was kept longer because she looked depressed and also we intended to observe whether the condition recurred or not; but it did not do so.

*Case 2.*—Child, age 5 months, was admitted into hospital on 2nd January, 1940, with extensive dermatitis on face, ears and neck. Pus showed staphylococci.

*History.*—Other children were playing with *Bhilawa* fruit. (Marking nut, *Bhela*.) Its juice fell on the face of the child making a few sores. Afterwards from the oozing of the sores, the surrounding parts became inflamed and the condition spread over the face, ears and neck. The possible explanation is that the original sores got infected with staphylococci which, in turn, set up extensive dermatitis. The front of the neck was worst affected.

The child was at once put on M. & B. 693 as follows:—

1st day	.. 3/4 tab. × 2
2nd day	.. 1/4 tab. × 3
3rd day	.. 1/4 tab. × 3
4th day	.. 1/4 tab. × 2
Total	2 1/2 tab., i.e., 1.25 grms.

The condition healed up rapidly and the case was discharged from hospital on 7th day.

By local treatment as mentioned in skin cases, I mean the application of one of the following generally, according to the case:—

(1) Lotio acriflavine 1 in 1,000.

(2) Unguentum hydrag. ammoniata.

(3) A lotion containing zinc sulphate grs. 6 and copper sulphate gr. 4 to an ounce.

In all cases the local treatment was continued while M. & B. 693 was being given.

As regards dosage we have always used it in smaller doses than that recommended by the makers, for pneumonia.

Points of interest:—

(1) the rapid control of temperature and toxæmia in pyelitis,

(2) the rapid healing up of skin conditions, none requiring more than 7 days.

My thanks are due to Dr. H. L. Slaughter for his guidance and for permission to read these case notes.





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more difficult because this side of drug manufacture needs large and expensively equipped laboratories and staffs of highly trained chemists and technicians. None of these things are beyond the power of India to furnish, as chemistry and physical science appear to have a special attraction to Indian scientists, and there are even now many chemists of high standing in this country, when the openings for employment with pay commensurate with their abilities are few. Should the prospects of this type of work improve no lack of suitable workers need be anticipated. India also has financiers and business men of imagination ready to put money into any industrial enterprise if a reasonable profit from their investments may be looked for.

The manufacture of drugs alone is not the only requirement, but it is even more important that the drugs made shall be up to the required standard and free from adulteration. Now that the war has forced upon us at short notice the urgency of an adequate supply of drugs to India it is all the more regrettable that Government was so slow to act on the findings of the Drugs Inquiry Committee's report, which, as long ago as 1931, showed the position of drug supply and manufacture in this country to be far from satisfactory. Nevertheless they did move eventually and made a beginning by the initiation of a Biochemical Standardization Laboratory in 1938; this is now busily engaged

testing medicinal substances on sale in India, and has already produced important results. This work is of the greatest value and will become of steadily growing importance as the manufacture of drugs and biological products in India increases, by forcing manufacturers to keep their products up to the necessary standard. This will eventually lead to it being greatly increased beyond its present small staff and strictly limited laboratory accommodation.

The present time appears to us as most opportune for pushing forward in India the manufacture of all kinds of heavy chemicals and their derivatives, the fine chemotherapeutic substances used so largely in present-day medicine, because there is the certainty that overseas supplies will be much restricted, if not altogether cut off for a time. This will mean that local drug manufactures can begin with relatively little competition from outside, a condition which will give them every opportunity of becoming firmly established. Then when the world returns to normal and international trade is freely resumed they will be able to withstand the competition from overseas, provided a reasonable protective tariff against foreign drugs is imposed; and if they have laid their foundations well they might even hope to capture a valuable export trade before the countries disrupted by war are again producing to full capacity.

## Special Articles

### REPORT OF AN ENDOCRINE CLINIC

By W. C. SPACKMAN, F.R.C.S.E., F.R.C.O.G.  
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#### I. Introduction

THROUGH the kindness of a number of firms which manufacture endocrine products (B.D.H., Boots, Ciba, Glaxo, Organon, Parke Davis, Schering), it was possible to open an endocrine clinic at these hospitals in February 1939. The clinic has now been working for just over a year and it is thought that a review of its work and some indication of its results may be of interest.

#### *Selection of cases*

Although there are many indications for endocrine therapy in the female, it is obviously useless to adopt a policy of widespread and almost uncontrolled administration, like giving a dose of an aperient or aspirin to the casual patient. Hormone preparations are very expensive and I consider manufacturers are not justified in giving even small amounts broadcast

as they do at present, to all and sundry, regardless of the proper selection of cases and control of treatment. One presumes that from the manufacturer's angle their best chance of increasing their sales is to accustom the average medical practitioner to the use of their particular product but the method has practically no scientific justification.

We have in our clinic made a very careful selection of cases treated and have controlled the administration by observation of results as long as possible. All cases are put on a special endocrine register under the executive charge of an individual member of the medical staff, and no patient is accepted unless (a) her case is considered entirely suitable for endocrine therapy and (b) she undertakes not to abandon treatment prematurely and irresponsibly. In spite of these precautions a number of cases have withdrawn themselves from our control before being discharged by us.

#### II. Hormones

The hormones used are as follows:—

1. Anterior pituitary hormones and other gonadotrophic substances.
  - (a) Follicle-maturing hormone ('prolan A').
  - (b) Luteinizing hormone ('prolan B').

(c) Lactogenic hormone, prolactin ('physolactin').

(d) Thyrotrophic hormone.

## 2. Ovarian hormones.

(a) Oestrogens.

(i) Natural.

(ii) Synthetic—Stilbœstrol.

(b) —Progesterone.

A few words on each of these is called for, indicating its source, its various forms, modes of administration, action and therapeutic uses.

The follicle-maturing hormone (prolan A) is derived from the serum of pregnant mares (gestyl, serogan, antostab). It is a complex substance, put up in dry form and administered after solution. Given intramuscularly it causes ripening of the graafian follicles; given intravenously it is said to cause their rupture if given near the date of ovulation. It is used for both these purposes, but it is not to be given where the ovary is above normal size otherwise it may cause the development of a cystic ovary by excessive ripening of follicles. In theory it is a most valuable product but its use must be carefully and intelligently controlled. We have used it with apparent success in cases of functional amenorrhœa, as detailed later in this paper.

Luteinizing hormone (prolan B) is derived principally from the urine of pregnant women. It is put up in liquid form (antuitrin-S) and as a powder for solution (gonan, pregnyl, prolan). It is administered by injection. It causes luteinization of the graafian follicle after the latter has ruptured, and in consequence the development of progestational changes in the proliferated endometrium.

Prolan A and prolan B therefore act primarily on the ovary.

Lactogenic hormone is prepared by a special process from the anterior pituitary and is put up in liquid form (physolactin). It is administered by injection. It increases mammary secretion and is given for this purpose.

Thyrotrophic hormone is also prepared from the anterior pituitary. It is put up as a powder (ambinon) for administration with or without prolan B by injection. It activates the thyroid and ovary and is used, for example, in fat women with amenorrhœa or hypomenorrhœa.

Oestrone is the follicular hormone of the ovary, which is also made by the placenta and occurs widely distributed in other tissues. It is made commercially from the urine of pregnant mares in which it is found in large amounts especially from the 4th to the 6th month. It is used plain (œstrone) or after esterification by which its action is intensified and prolonged (œstradiol benzoate and œstradiol dipropionate). It can be administered (a) orally as œstrone, (b) by injection in aqueous or more commonly in oily solution after esterification, (c) by injection, (d) by surface application in spirit solution, (e) by vaginal tablets or

pessaries, and (f) by implantation subcutaneously of pure œstrone tablets. It is placed on the market under about a dozen different trade names.

Stilbœstrol is a synthetic œstrogen. Although possessed of powerful œstrogenic action it is not at all closely related chemically to œstrone. It is used orally or by injection of the dipropionate for the same purposes as œstrone.

It may be expected that as a result of further experimental work other similar products will be introduced which will possess similar œstrogenic action and that such action may be in certain products specialized in certain directions so as to make a variety of artificial œstrogens available for treating a variety of clinical conditions at present treated uniformly with œstrone.

*Action and uses of œstrone and stilbœstrol.*—They produce :—

1. Enlargement of the under-developed uterus and mammary gland;
2. Proliferation of the endometrium and its glands;
3. Hyperœmia and proliferative thickening of the vaginal stratified squamous epithelium;
4. Depression in the activity of the anterior pituitary;
5. Sensitization of the uterine musculature to the action of pituitrin;

They have no direct action on the ovary.

Their uses are very numerous and include :—

1. Treatment of hypoplasia of the uterus;
2. Treatment of amenorrhœa, usually in combination with progesterone;
3. Treatment of cases of dysmenorrhœa due to hypoplastic (under-developed) uterus;
4. Treatment of senile vaginitis and kraurosis vulvæ;
5. Treatment of menopausal symptoms;
6. Treatment of missed abortion—not very practical as very large doses are required;
7. Treatment of uterine inertia and in the induction of labour;
8. Treatment of epimenorrhœa and of some cases of metropathia hæmorrhagica by inhibiting the action of the anterior pituitary and so delaying ovulation and subsequent menstruation;
9. Diminution and suppression of lactation, again by inhibition of the pituitary (prevention of its secretion of prolactin);
10. Promotion of the general metabolism of premature babies.

Progesterone is obtained from the corpus luteum of the ovary (usually of whales) but nowadays it is mostly prepared synthetically, as its chemical composition is known. It is administered by injection in oily solution, but recently a modification has been prepared which is active orally ('progestoral', and lutoeyelin oral).

Its action chiefly is :—

1. To produce progestational (secretory) activity in the endometrium after the latter has proliferated under the action of œstrone;
2. To favour therefore the embedding of the fertilized ovum;
3. To maintain a good decidua in pregnancy;
4. To prevent the premature action of pituitrin on the uterine muscle in pregnancy by antagonizing œstrone.

It is therefore used :—

1. In the treatment of amenorrhœa after a course of œstrone;
2. In the treatment of sterility, repeated and threatened abortion and to prevent premature labour;
3. To prevent 'after-pains';
4. In the treatment of functional menorrhagia by turning an unhealthily proliferated endometrium into a secretory one.

Although I have listed these different hormones as if they all had a separate and specific action, the functioning of the various endocrine glands is very closely interconnected, so that in nature the body is acted upon by a combination of the products of these glands in ever-varying amounts and usually with a species of rhythm. In healthy individuals these rhythms remain almost undisturbed; but in pathological conditions we are often very uncertain as to the exact ratio of disturbance of the various component hormones and therefore we may find it extremely difficult to correct the clinical picture. It is not merely a case of a gland secreting an excess or a deficiency of its own particular hormone but of the alterations in secretion thereby induced in other glands. Moreover, each gland may secrete, possibly, some modification of its own hormone, producing thereby effects not attributable merely to an excess or deficiency of its hormone (examples, Graves' disease, and acromegaly).

In this connection much experimental work is being done in the use of hormones from the testes and the adrenals and although at present the indications for using these hormones in a female endocrine clinic are not well defined, in some cases definite therapeutic effects have been produced by them where the apparently correct female hormone has been ineffective.

### III. *Classes of cases suitable for treatment and scheme of treatment planned*

#### *Disorders of menstruation*

*Amenorrhœa, primary.*—The most suitable cases are those of persons under 20 where moderate hypoplasia of the uterus and ovaries is present, which in fact might be considered as 'delayed onset of menstruation'.

#### *Diagnosis by biopsy*

An initial biopsy of the endometrium is undertaken to see whether a healthy endometrium is present and in what phase of development it is. In some cases a tuberculous endometritis is found and such cases are unsuitable for endocrine treatment.

*Endometrial biopsy* (E. B.) is so important a guide in our clinic that a few words on it are desirable\*.

We use either the Sharman or the suction type of biopsy curette. No anæsthetic is necessary with either, the specimens can be taken in the out-patient department and should be from the fundus if possible. They are placed at once in formalin saline. The best time to take them is just before menstruation is due or during the first few hours of the flow, because it is essential to find out whether the endometrium has reached the necessary secretory phase. A good secretory type of endometrium indicates a normally ovulating ovary and good uterine co-operation. The secretory phase is only developed from the proliferative phase in the last week, and the nearer we can run to the last day or hour the better.

Women can 'menstruate' without ovulation and we can produce the secretory phase followed by menstruation by hormone administration (œstrone followed by progesterone) but the normal source of these hormones is from the graafian follicle and its subsequent corpus luteum. It may be considered that there was no value in inducing menstruation of this type without ovarian co-operation simply by the use of ovarian hormones, but it is sometimes found, for reasons probably connected with the interaction and interrelation of the endocrine glands previously referred to, that the rhythm of menstruation is spontaneously re-established if it has been artificially produced two or three times. This may be presumed to be the result of rhythmic effects produced on the pituitary by the ovarian hormone, for we know that just as the anterior pituitary activates and controls the ovary so modifications of the ovarian hormones circulating in the blood are capable of modifying and of suppressing certain actions of the pituitary.

A much more natural process of producing menstruation is to aim at activating the ovary itself by the use of the hormones prolan A and prolan B secreted by the pituitary for this purpose, and it is probable that with prolan A and prolan B, modified perhaps as a result of further experimentation, we may cause a direct action on the ovary for the ripening and rupture of the graafian follicles and hence the consequent proliferative and secretory changes in the endometrium. It will be seen that we have attempted this method of producing menstruation apparently with success in one or two of our cases.

*Amenorrhœa, secondary,* can be similarly treated. Thyroid may need to be combined, or thyrotrophic hormone, in cases where hypothyroidism is a component.

To induce menstruation with hormones we give œstrone for a fortnight in full doses (but usually avoid the dipropionate whose action is too prolonged), and progesterone in the fourth week. We have had successes with prolan A (gestyl and serogan) giving it in daily doses for 3 days and expecting a period about 15 to

\* I am greatly indebted to Dr. P. V. Gharpurê, M.B. (Bom.), Professor of Pathology, Grant Medical College, for personally undertaking the examination of all our biopsy specimens and much of our work has been guided by his reports.

20 days later. We usually combine its administration with the simultaneous use of an oestrogen and it is possible that any success achieved is due to the latter rather than the former\*.

### *Epimenorrhœa*

Where the periods occur at too short intervals (this is much more often claimed to be so by patients than found by definite clinical observation) we try to delay the stimulus from the anterior pituitary, which causes the ovary to ovulate, by administering an excess of œstrone in the week following menstruation in order temporarily to inhibit the action of the anterior pituitary. The dipropionate should be used and appropriate doses are 5 mgm. daily for 5 days.

### *Menorrhagia*

Only functional menorrhagias are suitable for endocrine treatment and it must be established that a proliferated endometrium is present if any effect is to be expected from the use of progesterone or prolan B. In any case progesterone has to be used in very large doses in most cases and results are disappointing with both. It appears usually better to remove the irregularly hypertrophied and often cystic endometrium by curettage, and to try with œstrone followed by progesterone and prolan B to obtain a better type of endometrium. Some cases respond to large doses of œstrone and others to 'testosterone' or 'percorten' but results are by no means constant and failures are frequent. Such cases are usually much more safely treated by a hysterectomy if occurring near the menopause, or by partial oophorectomy if in young adults since they always show ovaries containing atretic enlarged follicles.

### *Dysmenorrhœa*

Where the uterus is hypoplastic, treatment with œstrone is indicated, and cases with a uterus of normal size may respond to progesterone. The latter is also very effective for relieving 'after-pains'.

*Menopausal syndrome*, including vaginitis, osteo-arthritis of middle age and pituitary headaches. These can be generally relieved by œstrone. Many of the symptoms, e.g., flushing, depression, sleeplessness can be almost entirely eliminated in most cases, and the treatment gives excellent results in senile vaginitis. Estradiol dipropionate or stilbœstrol is suitable for injection, and œstrone is one of its commercial forms, or stilbœstrol by mouth. The last named should not be given in doses over 1 mgm. twice a day and smaller doses are sometimes sufficient. We have used implantation of special compressed tablets of œstrone (kindly supplied by Organon) for menopausal cases and believe the method is of considerable value as

giving with one treatment, scarcely more severe than a hypodermic injection, a uniform absorption of œstrone lasting probably for several months. We have tried Kolpon tablets, which contain œstrone, but have found that some of our patients did not like them.

*Sterility*.—Assistance in treatment of functional sterility may be afforded by administration of œstrone, followed by progesterone or prolan B to promote the formation of a good endometrium and secure the embedding of the fertilized ovum in a well-developed progestational phase.

*Repeated abortion*.—The use of prolan B and of progesterone in the early weeks is well known and of proved value in preventing abortion. It may be combined with oral administration of vitamin E.

### *Disorders of lactation*

Painful engorged breasts can be relieved by giving œstrone in medium and repeated doses, and lactation can be entirely suppressed by the use of larger doses. We have also relieved conditions of chronic painful mastitis with testosterone.

Deficient lactation can be successfully stimulated by 'physolactin' but it would appear that the psychological co-operation of the patient is necessary if the good effect is to be maintained; this is not always forthcoming. The injections are continued in diminishing doses for several days. The effect is not impressive and begins within 24 hours, the injections occasionally are rather painful.

### *IV. Results of treatment obtained*

*Amenorrhœa, primary*.—Five cases were admitted for treatment and four received treatment, their ages being 18, 18, 17 and 15. Two were treated with œstrone and two with œstrone and prolan A; all responded to treatment and began to menstruate regularly.

*Example 1*.—Patient aged 18, moderate hypoplasia of the uterus and ovaries. E. B.: endometrium in resting phase. Treatment for two months with œstrone and prolan A resulted in six regular periods.

*Example 2*.—Patient aged 17, moderate hypoplasia of uterus and ovaries. E. B.: atrophic endometrium. Treatment: œstrone by injection and implantation of a tablet of œstrone, and with prolan A. Result: two regular periods.

*Amenorrhœa, secondary*.—Thirteen cases were admitted for treatment and ten received treatment; their ages being 35, 28, 27, 25, 21, 20, 20, 18, 18, 18.

Five obtained menstruation under treatment; Three did not obtain menstruation under treatment;

One result doubtful ('spotting');

One did not report following treatment.

*Example 1*.—Æt. 27. Amenorrhœa four years, following dilatation and curettage two or three times for irregular periods. Had part of an ovary implanted in 1936, no effect. E. B.: no endometrium obtained. Full treatment for several months with œstrone and prolan A. E. B.: still no endometrium. Endometrium was then grafted into her uterus from another patient,

\* These hormones will not produce abortion in any dosage, and I am not referring to the amenorrhœa of pregnancy.



but it was found that there was an old chronic salpingitis. No effect, treatment failed. This case illustrates the danger of promiscuous and probably vigorous curettage. I believe the lining of the uterus was entirely destroyed and replaced by scar tissue in this case and perhaps a salpingitis was induced in addition.

*Example 2.*—*Æt.* 25. Very fat. Amenorrhœa eight months. (Four sisters suffer similarly.) E. B.: early proliferation. Treatment with œstrone and prolan A and thyroid. No period obtained.

*Example 3.*—*Æt.* 21. Two and a half years' amenorrhœa. E. B.: endometrium, atrophic. Implantation of œstrone tablets  $2 \times 25$  mgm. on 11th October, 1939. Prolan A (gestyl) on 9th, 11th, and 13th December, œstradiol dipropionate  $4 \times 5$  mgm. with three doses of gestyl in January. E. B.: 24th January showed numerous glands with secretory changes. Menstruation two days later. Similar treatment in February gave another period. Continuing treatment.

*Example 4.*—*Æt.* 18. Eight months amenorrhœa, uterus hypoplastic. Fifty mgm. œstrone tablet implanted. No other treatment. Began to menstruate again two months later. Had one period then became pregnant and is now four and a half months' pregnant.

In some cases of secondary amenorrhœa one finds a small corpus luteum cyst on an ovary and its removal cures the condition.

*Oligomenorrhœa.*—Five cases were treated. Three, results doubtful; two satisfactory.

*Example 1.*—K. H., *æt.* 20, unmarried. Periods 3/60—90, scanty flow. E. B.: proliferative. L. P.: on 4th December. Treatment with prolan A (serogan) on 12th, 13th, and 14th January. Period on 4th February for four days. Treatment with prolan A (serogan) on 14th, 15th and 16th February—period on 3rd March for five days.

*Example 2.*—*Æt.* 25, one child, periods 1/30; getting stouter. Treatment with 'ambinon' (prolan B + thyrotrophic hormone) gave 3/30 periods and some loss of weight.

*Menorrhagia and metropathia hæmorrhagia.*—Five cases treated, one with slight improvement. One case turned out to be ectopic gestation.

*Example.*—K. H., *æt.* 16. Uterus normal. Bleeding for a month. Treated with prolan B and progesterone daily for 12 days. No effect. Dilatation and curettage gave immediate relief.

It appears that such cases should be immediately curetted provided the endometrium is found to be thick and hypertrophied, and subsequently rhythmically treated with appropriate hormones. If the ovaries are full of small cysts, they can either be resected or punctured very simply by posterior colpotomy. It appears to be rarely worth while giving treatment only with progesterone or prolan B or any other hormone, though some cases respond to such methods, but failures are very common even with very large dosage.

*Dysmenorrhœa.*—One case; hypoplastic uterus. Treatment for three months with œstrogens. E. B.: on 2nd August and 20th October, 1939, showed improvement in proliferative activity. Dysmenorrhœa was also much less. Discontinued treatment.

*Sterility.*—Four cases. Treatment designed to improve character of endometrium. Results uncertain.

*Vaginitis.*—Three cases, *æt.* 23, 22 and 19. All treated with œstrone. One with sulphanilamide. Results in all cases good.

*Senile vaginitis and pruritus.*—Seven cases, *æt.* 70, 54, 45, 45, 41, 39 and 37. Three did not keep in touch. Four markedly improved. Treatment given: œstrone by injection, implantation and inunction. Results very satisfactory. In two cases colporrhaphy was combined with the hormone treatment.

*Example 1.*—Patient *æt.* 54, complaining of acute itching leucorrhœa for the last ten years, much worse lately. Four children and five abortions. Menopause 12 years ago; mucous membrane of the vagina thin, pale and stippled. A thin discharge, containing many pus cells, few epithelial cells and no Doderlein bacilli. Rapid improvement with disappearance of symptoms. The patient refused colporrhaphy and will probably relapse as she has discontinued treatment.

*Example 2.*—*Æt.* 37. Menses still present but scanty and infrequent. Much pruritus and typical atrophic vaginal mucous membrane. Treatment with stilbœstrol and implantation of œstrone tablet for two months. Result: cured.

*Menopause.*—Four patients. Two natural menopause, *æt.* 43 and 40; two post-operative, *æt.* 33 and 30. All treated with œstrone or stilbœstrol. Two by implantation and injections and two by injections only.

*Example 1.*—*Æt.* 43; very depressed and neurotic. No improvement in mental condition but marked improvement in vaginitis.

*Example 2.*—*Æt.* 40; flushes, depression, headaches—all markedly improved by injections and oral treatment (stilbœstrol).

*Example 3.*—*Æt.* 33; bilateral oophorectomy. Flushes ++. Symptoms entirely relieved.

*Example 4.*—*Æt.* 30; bilateral oophorectomy and prophylactic implantation of œstrone tablet; menopausal symptoms did not develop.

*Genital hypoplasia.*—One case *æt.* 20, treated with œstrone. Result?

*Habitual abortion.*—Four cases: two did not continue treatment; two treatment successful.

*Example 1.*—History of three abortions, no full-term pregnancy. Two months' pregnant, put under treatment until end of 4th month with progesterone and delivered of a full-term living child.

*Example 2.*—Three full-term normal deliveries followed by four spontaneous abortions, then one full-term normal delivery whilst under treatment with progesterone in 1938. Another abortion in 1939, no treatment; later in 1939, came at three months with slight bleeding. Treated with *progestoral* 5 mgm. daily for eight days and then on alternate days for two months. Delivered of a living child at full-term.

*Hyperemesis gravidarum.*—Three cases, treated with *progestoral* and luto-cyclin oral. Two reported marked improvement, one uncertain.

#### *Infantile debility and prematurity*

For this experiment 12 sets of twins were taken and the smaller of each pair was given œstrone orally every day in doses up to 100 units three times a day. There was no indication whatever of any beneficial effect.

*Deficient lactation.*—Seven cases. Five treated within first ten days of delivery; two successful; two temporary success; one failure. Two treated at about 3rd month of lactation owing to failing activity of breasts; both successful.



*Example 1.*—*Et.* 27, delivered by Cæsarean section on 23rd August, 1939; very scanty secretion; Physolactin on 2nd, 4th, 5th, 6th and 7th September. Result slight improvement; case recorded as a failure.

*Example 2.*—*Et.* 31; delivered 12th August, 1939. No activity at all in breasts on 5th day; Physolactin on 16th, 17th, 18th, 19th, and 20th August. Gave copious secretion which continued fully adequate for some weeks.

*Example 3.*—*Et.* 35; diabetic. Delivered by Cæsarean section. No secretion on 5th day; Physolactin resulted in good secretion but the patient appeared to favour bottle-feeding and her milk soon failed.

*Example 4.*—*Et.* 31. Japanese. Very insufficient milk during 4th month of lactation. Patient anxious to continue lactation as she was shortly returning by steamer to Japan. Physolactin gave fully adequate supply for large vigorous child well maintained into the 7th month; still continuing.

*Excessive secretion.*—Patient *act.* 32 with excessive milk supply established two days after delivery. The supply was diminished successfully by injections of stilbæstrol dipropionate 1 mgm. twice a day for four days. Later the milk supply again became excessive and was again reduced by similar means.

#### V. Summary and conclusions

I would like to emphasize that in considering our patients in an endocrine clinic we must not

lose sight of the fact that in all cases great importance must be attributed to questions of diet and general hygiene of healthy living, as well as to the correction of anæmia and any other adverse symptoms discovered. It is certain that many cases at first thought to be suitable for endocrine therapy, can receive far more benefit if the hormone administration is combined with suitable general treatment, in fact in many cases all that may be needed is the latter.

In the following summary I have not tabulated the list of conditions which can theoretically be benefited by endocrines but those in which such treatment has appeared to us usually to be worth trying. I have therefore excluded conditions such as the functional hæmorrhages, the 'metropathias' and functional menorrhagias where the results seem to be bad even with such enormous doses of endocrines that very few patients could dream of undertaking them in view of expense alone.

Biopsy control is necessary in the amenorrhœa and sterility cases, and vaginal smear in all types of vaginitis.

#### Summary

Condition	Scheme of endocrine therapy	Summary of our results
<i>Gynæcological</i>		
Primary amenorrhœa with genital hypoplasia.	Small repeated doses of œstrogens with short intermittent courses of gonadotrophic hormones <i>e.g.</i> , for the former 1 mgm. of dipropionate of œstradiol twice a week, and three doses of follicle-ripening hormone at one-day intervals once a month. The latter not to be repeated more than twice without re-examination and biopsy.  The œstrogen may be stopped and progesterone given in three doses of 2 mgm. each on alternate days. Ten days after the follicle-ripening hormone and menstruation expected at the conclusion of this.	Favourable.
Secondary amenorrhœa and oligomenorrhœa.	Follicle-ripening and luteinizing hormones (plus thyroid if indicated).	Favourable in absence of organic disease.
Sterility .. ..	As for primary amenorrhœa but control by biopsy is absolutely essential. (All other usual methods of investigation and treatment to be adopted as required.)	
Epimenorrhœa .. ..	Four or five doses of 5 mgm. each of dipropionate in the week immediately following the period.	Favourable, but the period may be considerably delayed so that the patient thinks she is pregnant.
Menorrhagia .. ..	Heavy doses of luteinizing hormone and/or progesterone.	Unsuccessful; we do not recommend endocrine treatment at present for functional bleeding.
Dysmenorrhœa— (i) With genital hypoplasia	Small repeated doses of œstradiol dipropionate throughout the month, not sufficient to inhibit the pituitary, continued for several months.	Appears to help in properly selected cases.
(ii) With normal-sized uterus	Progesterone at time of periods.	

*Summary—concl.*

Condition	Scheme of endocrine therapy	Summary of our results
<i>Gynaecological—concl.</i>		
Senile vaginitis ..	Œstrogens in full doses by all usual modes of administration. If stilboestrol is used, begin with 1 mgm. per day as patients are not always tolerant of it.	Very helpful.
Menopause ..		
Pruritus vulvæ ..		
<i>Obstetrical</i>		
Threatened abortion ..	Progesterone in full doses, followed with smaller continued doses. Luteinizing hormone may be added in first three months.	Worth trying where symptoms are not hopeless.
Repeated abortion ..	Luteinizing hormone and progesterone in moderate doses right up to 7th or 8th month. Progesterone or lutoecyclin oral may be substituted for injections. Two milligrams by the mouth equal one by injection.	Good.
Hyperemesis gravidarum ..	Progesterone or lutoecyclin oral (some advise œstrogens but we have not found them helpful).	Appeared helpful in several cases.
Infantile debility ..	Œstrogens	No success.
Uterine inertia ..	Œstrogens in large doses	No apparent success, but it is theoretically useful.
Deficient lactation ..	Physolactin 5, 5, 2, 2, and 1.0 c.cm. on successive days.	Results most encouraging.
Excessive lactation ..	Œstrogens	Results most encouraging.
After-pains ..	Progesterone	Very effective.

## AGAINST ORTHODOXIES IN SYMBOLISM, MICROMETHODS AND MICROMATHEMATICS

By S. D. S. GREVAL  
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### I. SYMBOLISM

'LET T represent the dominant character tall and t the recessive character dwarf' says almost every author (latest available example Ride, 1938) yearning to impart the necessary Mendelian knowledge to the would-be genetician or even to the humble seeker after truth in respect of the incidence of blood groups and its application to the disputed paternity or maternity of an offspring. Let nothing of the kind be done. If T represents the dominant character Tall, d should represent the recessive character dwarf. For exactly the same reason if Y represents the dominant character Yellow, g should represent the recessive character green. There is no particular merit in being cryptic and using a code when plain language will do and in fact do better. Decoding and following the formation of new combinations at the same time is irksome to say the least.

Further, it has been known for many years that the dominance and the recessiveness of characters are conditioned by the environment. Supposing by a change in environment tallness became recessive and dwarfness became dominant, how would the characters be

represented then, and how would anybody understand what had happened?

Nothing but unnecessary crypticism is responsible for representing the dominant Red eye of the female fruit fly (*Drosophila melanogaster*) by W.

Segregation of contrasting characters and production of the dominant form in the offspring is as easy to follow as deciding who won a trick in a game of cards, provided the crypticism is kept out. Thomson (1934), an eminent biologist of a bygone age, decided to discard it in his latest publication. It should be discarded by everybody. It is a wilfully introduced embarrassment in the consciousness.

### II. MICROMETHODS

#### 1. Estimation of the life of a red corpuscle

This was done by an estimation of bilirubin supposed to be formed in a given time. The estimate gave the life of the human corpuscle as 30 to 40 days (Evans, 1925). The actual life of a transfused corpuscle of the same group but not of the same type as the recipient's red blood cells, detected by immunological means, extends over 100 days (Levine, 1935). It is reasonable to suppose that when the donor and the recipient belong to the same group and the same type the life of the transfused corpuscle is prolonged further. The life of a subject's own corpuscles must be longer still. It must be more like 365 days than 30 to 40 days.

The group specific substances in the red blood cells are the isohæmagglutinogens A and B while

the type specific substances are the hæmagglutinogens M and N (for details see Greval, Chandra and Woodhead, 1939; Greval and Chandra, 1939).

The estimate of 30 to 40 days was a very bad estimate indeed.

## 2. Minute mathematical calculations

One of the pieces of evidence regarded as most incriminating to Sacco, in the Sacco and Vanzetti case of U. S. A. notoriety (Kamath, 1938), was that of a gun expert who proved by 'minute mathematical calculations' that the marks in the bore of Sacco's gun were made by the bullet which killed the murdered man. Later another man called Milazzo was accused in Cleveland (Ohio) of having shot someone else. The same gun expert again demonstrated that the shot was fired from Milazzo's gun. Fortunately, the maker of the gun was able to prove that it had not been sold until a month after the murder! But Sacco and Vanzetti had by that time been executed.

The original American description is not available. The usual method is to look for marks made on the bullet by the barrel, not to look for marks made on the barrel by the bullet. No two barrels being exactly alike, a 'gun print' comparable to a finger print is left on the bullet. The fact, however, remains that, at least in the second case, the gun expert, going by 'minute mathematical calculations', made a mistake. But for the ordinary evidence the expert's evidence would have led to a miscarriage of justice. It is as likely as not that his evidence did lead to a miscarriage of justice in the first case.

In *Rex v. Ruxton* case (Manchester Assizes, March 1936) Brash's evidence (Smith, 1938; Glaister, 1938; Blundell and Wilson, 1937) on the identification of the skulls presumed to be of the missing women was a distinct advance in forensic medicine. Photographs of the skulls when superimposed on life-size photographs of the heads of the two women showed a remarkable degree of fitting in each case. Yet Brash was careful to point out that this did not imply positive identity but only indicated that the skulls could belong to the missing persons. Such should be the attitude towards evidence which is based on items of minute dimensions or is not exclusive enough.

Positive evidence on handwriting cannot be superior to Brash's evidence. Negative evidence has been known to deceive experts. A student's handwriting obtained as a sample, when he was in custody, did not correspond to the writing on an incriminating document. Earlier in custody he had made an application to sit for the examination for which he had been studying. This was granted. The writing on the application, the answer papers and the incriminating document was identical (Lucas, 1935). In about a month's time he had practised and perfected a disguised hand.

The detection of forgery, incidentally, is a different and usually an easy matter. As a rule the fingers of the forger move with hesitation, which is apparent on enlarging the writing and comparing it with the enlarged original. Some forgers, however, can get over the hesitation, with practice, in forging a small number of words, such as is needed in forging a cheque.

## III. MICROMATHEMATICS

### 1. Mathematics and micromathematics

That averages should be corrected for probability; that a rupee when tossed with the same balance and force will give as many heads as tails, only when the number of tosses is large; that fluke chances turn up; and that the chances with a rupee are essentially different from those with a dice, we are pleased to know. We will even buy books and renew our acquaintance with algebra and differential calculus. This is mathematics. That figures must be plotted on complicated curves; that equations well stocked with f's, d's and v's should be constructed; and that many letters of the alphabet should be distorted or dislocated to represent something or other in the process of calculation, before we as medical men, in a surgery, ward or laboratory, can say or do anything we may not consider significant. This is refined or micromathematics, which is a further obfuscation of the minute mathematical calculations referred to above. So far as our activities are concerned it is a figment of the mathematicians.

### 2. Advances in medicine are independent of micromathematics

None of our advances in medicine, surgery, anaesthetics and therapeutics has had the remotest connection with micromathematics. Even our laboratory work in subjects like physiology and pathology has progressed very well without it (and in recent years in spite of it). This is due to the fact that protoplasmic organisms do not live, grow, decay or die along complicated curves.

An outstanding example of the failure of even simple arithmetic to account for a well-known biological occurrence is found in Mendelism. The nearest approach that Mendel could make to his 3 : 1 ratio, in a life time, was 2.84 : 1.

Another, even more outstanding, example of the failure of simple arithmetic occurs in immunology in the following relationship between the diphtheria toxin and its anti-toxin :—

(1) A minimal lethal dose (M.L.D.) of diphtheria toxin is the smallest amount which kills a guinea-pig weighing 250 grammes in 4 days.

(2) A completely neutralized dose ( $L_0$ ) is the largest amount of toxin completely neutralized by 1 unit of diphtheria anti-toxin.

(3) A re-toxicated dose ( $L_+$ ) is the smallest amount of toxin which when mixed with 1 unit of diphtheria anti-toxin just kills the standard

animal in the standard time. In other words, it acts like 1 M.L.D.

Dose (3) minus Dose (2) should be equal to Dose (1)

or

$L_4$  minus  $L_0$  should equal 1 M.L.D.

In actual practice  $L_4 - L_0 = 8$  to 12 M.L.D. (Hewlett and McIntosh, 1932).

The same looseness of relationship exists between all toxins and their anti-toxins.

3. *The figment of the mathematicians does not appear to be used even in important human activities of peace and war*

The producer of the raw material mostly works without machinery and has little scope for mathematical refinements. The manufacturer of goods works with machinery yet uses very little mathematics. The seller of the goods prefers advertisement and creation of demands to the statistical analysis of the existing demands. Even if the first two categories of workers were supplied with micromathematically perfect machinery, only the production will be increased, not the distribution of the product. An increase in production without an increase in distribution does not lead to national prosperity or international amity.

In sport, judging of form, handicapping or even forecasting of events by the professional advisers is not based on a complicated system of calculation at all. If the existing system were faulty the refined mathematicians would have the wealth of all the 'totalisators' in the world at their disposal. Such is not the case.

When the leaders of nations choose between peace and war they do not do so in an atmosphere of higher and pure mathematics.

### Summary

1. Crypticism in symbolism is a wilfully introduced embarrassment in the consciousness.
2. Important findings should not be based on micromethods. The latter may be particularly dangerous in their application to forensic matters.
3. Complicated mathematics has no place in biological processes. It has no place even in collective human conduct in peace and war.

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## Medical News

### THE DRUG AND PHARMACEUTICAL INDUSTRY IN INDIA

'THE drug and pharmaceutical industry in India has developed considerably and in order to enable it to make further headway, simultaneous growth of heavy and fine chemical industries and industries connected with coal carbonization and production of solvents, etc., is essential. If the required basic materials and chemicals are readily available, it is possible to produce in India all the drug requirements of the country.' This is the conclusion of the 'Medical Preparations' Sub-Committee of the Indian Chemical Manufacturers' Association, Calcutta, in their report recently submitted to the Government of India. It is stated that India possesses a wonderful range of vegetable materia medica and nearly three-fourths of the drugs mentioned in the British Pharmacopœia grow in this country in a state of nature and the remaining one-fourth can be easily cultivated in some part of the country or other. In the appendices to the report, the sub-committee have included two lists, (1) Drugs belonging to the British Pharmacopœia which grow in India and (2) those included in the British Pharmaceutical Codex and the Extra Pharmacopœia which either grow spontaneously or can be easily grown. It is the opinion of the sub-committee that if due attention is paid to the proper cultivation and utilization of vegetable drugs, India would not only be completely self-supporting in this

respect but would also be able to develop an export trade in crude vegetable drugs. The sub-committee refer to the position about the production of oils, including essential oils, fixed oils and liquid paraffin; alkaloids including caffeine and its derivatives, emetine, morphine and codeine and their derivatives, strychnine, ephedrine, quinine, glucosides including digitalis; inorganic and organic drugs, inorganic and organic metallic compounds; synthetic chemo-therapeutic products, organo-therapeutic products; coal-tar products; biological products including sera, vaccines, bacteriophage, etc.; vitamin preparations, patent foods, surgical dressings, disinfecting fluids and other miscellaneous requirements. The sub-committee have also appended lists of essential drugs and medicinal chemicals available in India, of drugs and medicinal chemicals of secondary importance available in India, of basic chemicals necessary for the manufacture of drugs and the possibilities of their manufacture in India and tables showing imports of drugs, patent and proprietary medicines and chemicals along with their industrial uses. The sub-committee invite the attention of the Government to the necessity of close co-operation between the drug manufacturing concerns and hospitals. At present the manufacturers in India find it difficult to make a clinical trial of their products in any hospital under the Government and semi-Government bodies and it urges the State to render necessary help in this respect.

The sub-committee was presided over by Brevet-Colonel R. N. Chopra, Director, Biochemical Standardization Laboratory, Calcutta, and consisted of the following members:—Mr. J. N. Lahiri, Dr. H. Ghosh, Dr. B. N. Ghosh, Dr. U. P. Basu, Dr. B. C. Guha, Dr. I. B. Basu, Dr. B. Mukherjee and Mr. S. R. Dhadda, Secretary, Indian Chemical Manufacturers' Association (*ex-officio*).

### THE XVII ALL-INDIA MEDICAL CONFERENCE, 1940, VIZAGAPATAM

THE SEVENTEENTH ALL-INDIA MEDICAL CONFERENCE will be held at Vizagapatam (Waltair) in the last week of December 1940. The Reception Committee is anxious to improve the standard and utility of the scientific section.

Members of the Indian Medical Association or other Registered Medical Practitioners may present one or more papers at the session, provided they enlist themselves as members of the conference or of the scientific section.

Those who propose to read papers should forward them together with three copies of abstracts of the papers so as to reach the Chairman of the scientific section not later than 15th October, 1940, for submission to the scientific committee. Abstracts should be type-written and must not exceed 200 words. They should not include formulæ or diagrams. It might not be possible to allot more than ten minutes for the reading of any paper. Intimation of the acceptance of the paper will be communicated one month before the actual session of the conference.

P. KUTUMBIAH,

*Chairman, Scientific Section.*

MAHARANIPETA P. O.,  
VIZAGAPATAM.

### THE CALCUTTA PUBLIC MEDICAL SERVICE SCHEME

WE publish below the details of a scheme for contract medical service to persons of limited means. This scheme we are informed was approved by the Calcutta branch of the Indian Medical Association in November last. Though such a scheme is undoubtedly a move in the right direction it is doubtful if the present time is opportune for its inauguration:—

I. *Name*:—The Calcutta Public Medical Service.

II. *Aims and objects*:—

1. The system of Medical Service is a contract medical service directed to the achievement of positive health and the prevention of diseases no less than to the relief of sickness.
2. There should be provided for every individual the services of a general practitioner or a family doctor of his own choice.
3. Consultants and specialists, laboratory services and all auxiliary services together with hospital provision when required should be available for the individual patient normally through the agency of the family doctors.

III. *The availability of the service*:—

1. It would be desirable to fix income limit for persons intending to join the scheme. This income limit may be set at Rs. 250 per month and a graded scale of fees should be charged.
2. Attempts should be made by the Central Public Medical Service organization to move the Calcutta Corporation and the Government to enact necessary legislative measures whereby all of their employees coming under the above income limit will have to join the scheme compulsorily.

3. Persons with an income above Rs. 250 per month may join the scheme on application to the Central Organization with limited facilities.

### IV. *Rules and regulations*:—

1. All contributions are payable in advance according to the following schedule:—
2. *Schedule*:—
  - (a) Contributors with monthly income below Rs. 100 shall pay Rs. 3 per quarter for self and Annas 12 as per quarter for each dependant.
  - (b) Contributors with monthly income between Rs. 100 and Rs. 250 shall pay Rs. 6 per quarter for self and Rs. 1-8 for each dependant.
  - (c) Contributors with monthly income above Rs. 250 may join the scheme on application to the central organization and on certain conditions.
3. In exceptional cases, the clinic may allow payment of contributions in monthly instalments *pro rata* after the first quarterly payment.
4. The contributors are entitled to free medical service (exclusive of supply of medicines and appliances) at their respective clinics during their specified surgery hours.
5. A contributor is also entitled to medical service at his residence on the following conditions:—
  - (a) The illness is of such a nature that in the opinion of his physician the patient is incapable of attending the clinic personally.
  - (b) The clinic is informed by the party concerned before 9 a.m. that a visit is required (except in cases of emergency).
  - (c) The contributor agrees to pay for calls made between 9 a.m. and 9 p.m. a sum of Annas 8 or Annas 12 per visit according as his residence is within three miles or over three miles respectively from the clinic.
  - (d) The contributor agrees to pay Rs. 2 and conveyance charges for all visits (night calls) made between 9 p.m. and 9 a.m.
6. The charges for residential calls as specified above are payable in cash at the time of the visit. The clinic may however allow monthly adjustments provided payments are made before the 10th of the next month failing which the clinic may suspend all privileges to the defaulting contributor and his dependants.
7. If a contributor fails to pay his quarterly contributions within a fortnight of the due date, his status as a contributor will cease on that date, and he will not be re-admitted unless he pays a re-admission fee amounting to half his quarterly contribution.
8. In case of monthly contributor the period of grace will be one week from the due date of payment, *viz.* the third day of every month, and the re-admission fee shall be equivalent to one month's contribution.
9. If a contributor and his dependants have not availed of the services of the clinic during the previous quarter, he shall be entitled to a ten per cent rebate of his usual contribution fee.
10. The clinic reserves the right to refuse admission or re-admission to any applicant without assigning any reason.
11. All enquiries should be addressed to the Honorary Secretary, Calcutta Public Medical Service Scheme, Indian Medical Association, Calcutta Branch, 67, Dharamtala Street, Calcutta.

V. *Benefits conferred by the scheme:—*

1. The nature and scope of medical service to which the contributor and his dependants are entitled includes 'all proper and necessary medical services other than those involving the application of special skill and experience which general practitioners as a class cannot reasonably be expected to perform'.
2. Medical service to contributors does not include the supply of medicines and appliances.
3. Attendance in labour and attendance within 10 days after labour, in respect of any condition resulting from labour is not within the purview of the scheme. Antenatal care and the treatment of any condition not arising out of labour are covered by the scheme. Premature delivery before twenty-eight weeks of pregnancy is also covered by the scheme.
4. Cases of cholera, smallpox and cerebro-spinal meningitis which require institutional care will only be treated by the clinic pending their removal to a hospital for such cases.
5. All minor operations such as can be reasonably performed by a general practitioner and do not require special skill will be done free of charge at the clinic or at the patient's residence as the case may be.
6. Administration of the anæsthetic or other assistance at an operation will be undertaken free of charge by the clinic doctor if the said services do not involve a degree of special skill or experience not possessed by general practitioners as a class.
7. Laboratory and other special services such as radiological investigation, dental and ophthalmic services, etc., if required, shall be arranged by the clinic at the specially reduced rates recommended by the Indian Medical Association, Calcutta Branch.
8. The consultant's and specialist's services, if required, shall be arranged by the clinic from a panel of consultants and specialists at the reduced charges recommended by the Indian Medical Association, Calcutta Branch.

VI. *Administration:—*

1. The Medical Service is thrown open to the whole of the medical profession. Accordingly any medical practitioner registered under the provisions of the Bengal Medical Act, 1914, is entitled to work under the Calcutta Public Medical Service Scheme as one of its unit, provided that he abides by the rules and regulations of the Scheme as framed, altered and modified from time to time by the Indian Medical Association, Calcutta Branch.
2. A Central Committee shall be formed for the general control and co-ordination of the economically independent units working in different parts of the city.  
The Central Committee shall consist of—
  - (a) President of the Calcutta Branch, I. M. A.
  - (b) President of the Bengal Provincial Branch, I. M. A.
  - (c) Honorary Secretary, Calcutta Branch, I. M. A.
  - (d) Honorary Secretary, Bengal Provincial Branch, I. M. A.
  - (e) One representative from the Calcutta Medical Club.
  - (f) One representative from the All-India Medical Licentiates' Association, Calcutta Branch.
  - (g) Five representatives from the Executive Committee, Calcutta Branch of the I. M. A.

(h) Three representatives from Panel Doctors.

(i) Three representatives from amongst the Contributors.

3. The Central Body shall be responsible for the working of the scheme. All constituent units have to be recognized by the Central Committee before they can function.
4. All disputes and difficulties arising in course of working of the scheme are to be reported to the Central Committee, whose decision in such matters will be final.
5. The Central Committee shall have power of disciplinary action against constituent units.
6. The Central Committee shall form in a joint meeting with the Executive Committee, Calcutta Branch of the I. M. A., a Board of Consultants and Specialists, the duty of which will be to establish a list of consultants and specialists who satisfy a certain standard of eligibility and who desire to render service under the Scheme.
  - (a) It is suggested that the consultant and specialist's service should be available only on the recommendation of the family doctor and a fixed concession fee recommended by the Calcutta Public Medical Service, Central Committee, should be charged for such a consultation or specialist's service.
  - (b) It is suggested that the consultant and specialist's service to be available should be defined as such examination as can be given at a single consultation together with a report, where necessary, for the information of the attending practitioner.

## NUTRITIVE VALUE OF RICE

ANOTHER Bulletin dealing with nutritional questions has been published in the Government of India Health Bulletin Series. This has been prepared in the Nutrition Research Laboratories, Coonoor, and has been approved by the Nutrition Advisory Committee of the Indian Research Fund Association. An earlier Bulletin (No. 23) entitled 'The Nutritive Value of Indian Foods and the Planning of Satisfactory Diets' proved very popular and some 35,000 copies of the first and second editions have been sold or distributed. This bulletin was concerned with Indian foods in general. The new bulletin (No. 28), entitled 'Rice', deals in detail with the nutritive value of rice and the defects of the poor rice eater's diet.

Rice is the staple food of about half the human race. In India the area under rice exceeds that under all other cereals put together. Diet surveys have revealed the composition of the rice-eater's diet, showing that he consumes, in addition to his staple cereal, only very small quantities of such foods as pulses, vegetables, fruits and meat. Milk and milk products are taken in negligible quantities, or not at all. In the circumstances the nutritive value of the main ingredient in the diet is of primary importance.

The bulletin describes the effect of milling on rice. The outer layers of the grain are richer in vitamins and other materials than the inner starchy part. Hand-pounding removes some of the outer layers, but does not very greatly impoverish the nutritive value of the grain. But when raw rice is machine-milled, there is a serious loss of vitamins and particularly of vitamin B<sub>1</sub>, which prevents and cures the disease beri-beri. But parboiled rice, even when highly milled, retains most of the anti-beri-beri vitamin originally present in the unmilled grain.

The steaming to which the grain is subjected during the parboiling process causes vitamin B<sub>1</sub>, and a number of other valuable food constituents, to diffuse through the grain, so that they cannot be removed when milling subsequently takes place. The washing of rice removes



a considerable amount of food material, including about 50 per cent of vitamin B<sub>1</sub>. Cooking with excess of water also reduces the nutritive value.

A section is devoted to beriberi and it is shown that this disease is a serious public health problem in only one part of the country—the Northern Circar districts of the Madras Presidency. The reason for this is that in this area the poor prefer raw rice. Elsewhere in India polished rice is usually eaten and this contains enough vitamin B<sub>1</sub> to prevent beriberi.

The bulletin describes an investigation of the milling problem in the Madras Presidency. It was found that about 70 per cent of the population now consumes machine-milled rice. The underlying factors were found to include the following. The rice mill has spread everywhere and the people have come to regard it as a labour-saving convenience. Small holders are often faced by poverty and debt and dispose of their paddy to merchants and do not retain sufficient for their own use, a large proportion of the poorer section of the community lacks accommodation for the storage and pounding of paddy, paddy cannot be purchased in small quantities for pounding, when home-pounded rice is put on the market is in article of commerce it is dearer than machine-milled rice because of the labour costs involved. At present such rice reaches the market only in very small quantities.

Ways and means of improving the poor rice-eater's diet are considered. The nutritive value of the staple itself can most easily be raised by preventing the losses occurring in milling, washing and cooking.

It is important that the effect of parboiling in minimizing losses on milling should be generally recognized. Legislative action to check the spread of rice mills, or to reduce the number already in existence, is not recommended. What can and should be done throughout India is to educate people about the food value of rice in its various forms. Everybody should have a clear idea of what happens during the milling, washing and cooking of the most important food in the country.

Finally, 'supplementary' foods are discussed. The actual diet of the poor rice-eater and a well-balanced diet are compared and it is shown that the former contains too little milk, pulses, vegetables, and other foods. Milk supplies many of the food factors in which rice diets are deficient. Skimmed milk and butter-milk of good quality are valuable supplements. The partial substitution of rice by one of the millets, particularly *ragi*, improves poor rice diets. The bulletin stresses the need for the increased production of vegetables, especially green leafy vegetables and urges the development of the fishing industry.

#### WELFARE WORK FOR SOLDIERS' FAMILIES

A STEADY increase in welfare work among the families of Indian soldiers shows that difficulties of caste, class and religion are now interfering less than in the past.

Demands for treatment are becoming more general and it is frequently suggested that the treatment of families of Indian troops and followers and the provision of hospitals may shortly have to be recognized as an obligation of the central authority. One solution suggested is the allotment of portions of Indian military hospitals. While this may be possible where spare buildings exist the authorized provision of beds for troops and followers may at times be fully required.

At present, apart from certain payments of wages and provision of personnel, the whole welfare and family treatment system is done by voluntary effort by subscriptions from units, by donations from central charitable funds and by personal and financial support of the wives of officers of the units concerned. Much voluntary work is done by medical officers and the members of the Indian Medical Department.

There are now some 80 welfare centres. At all the centres the numbers attending in 1938 were approximately 84,677 women and 100,367 children. The progress of the work is dependent largely on the money available. The demands for accommodation, trained personnel and treatment are continually increasing.

In several big stations difficulty has been experienced in obtaining suitable lady assistant surgeons and qualified nurses.

Accommodation is usually provided in converted married quarters which are quite suitable for small units. In larger stations the practice is to establish family hospitals and have welfare centres included in the hospital buildings and activities. In a few stations welfare centres provide only outdoor treatment and arrangements are made with neighbouring mission hospitals, charitable general hospitals or civil hospitals to deal with hospital cases.

In addition, several amenities for women and children are being provided in the way of playgrounds and schools, purdah gardens for the women and even hot-water bathing establishments.

In most centres subscriptions from men, from the unit funds, and from officers and their wives make up from two-thirds to three-fourths of the resources of the welfare centre. The Maternity and Child Welfare Bureau and the provincial branches of the Indian Red Cross Society make grants-in-aid to the best of their ability.

Where beds are available women are making greater use of such accommodation for confinements with beneficial results.

#### LESS SANDFLY FEVER AMONG TROOPS

THE persistent fall in sandfly fever among troops has been noticed by Army Health authorities in India. This is said to be largely due to preventive measures.

Admissions in Landikotal, a hotbed of sandfly fever, which stood at 239 cases in 1935 dropped to 19 cases in 1938.

While the reduction here may perhaps be due to the fact that some of those forming the garrison during 1938 came from outer parts of the Peshawar district and were presumably 'salted' troops, the major part of the decrease can be put down to the use of 'Pyefly' spraying in barracks, to the co-operation of the troops in anti-sandfly measures, and to the replacement of the old mud buildings by modern stone or concrete ones. The canalization and making 'pukka' of nullahs as far as they can be improved has also helped.

Sandfly fever in the Northern Command dropped from an incidence of 36.04 per thousand in 1929 to 7.10 per thousand in 1938. Spraying and fumigation, resorted to as anti-malarial measures, have incidentally done much to bring about this reduction in the incidence of sandfly fever.

#### WORK AT THE KASAUJI MILITARY FOOD-TESTING LABORATORY

SOME idea of the care which the army takes to see that the soldiers in India secure wholesome food and good supplies can be obtained from the work done at the Military Food Laboratory, Kasauli. In 1938 alone a record total of 18,012 samples was examined.

In several cases tinned milk with high acidity in inferior tins, pearl barley coated with mineral water in inferior tins, highly polished rice, parboiled and broken rice and indifferent biscuits had to be rejected.

The main cause of rejection was the inability of manufacturers to realize the high quality required.

The samples from abroad are mainly from Australia which produces good supplies with only 1.2 per cent rejections. Australian jams have been found to be better in quality than those from the United Kingdom.

The Indian products are not satisfactory. Indifferent stocks of biscuit, salt, pearl barley, rice, bran and even sugar are submitted in the hope that the mixed inferior grades will be accepted.

Special biological assays were undertaken—the vitamin-'C' content of ascorbic-acid tablets for protection against scurvy and the phosphorus pentoxide specification for rice was investigated.

A dietetic survey of the Lawrence Military School, Sanawar, was carried out and certain improvements brought into force as a result.

Food contamination in connection with chemical warfare has been studied and further work is in progress. The superchlorination of water for drinking purposes has been tested and a special report is being prepared on the subject.

Revision of the Royal Indian Army Supply Corps specifications was carried out and the pamphlet on 'The Method of Submitting Samples' was revised and brought up to date.

Many improvements were carried out in the equipment and fittings of the Ghee Heating Centre at Agra. The number of samples submitted to the centre was 3,973. In general, the ghee was satisfactory, but the average acidity was high and there were three rejections for high acidity. Three thousand nine hundred and seventeen samples were finally accepted.

#### THE PHARMACEUTICAL AND ALLIED MANUFACTURERS' AND DISTRIBUTORS' ASSOCIATION, LIMITED

THE first ordinary general meeting of the above association was held on 12th July and office-bearers were appointed.

#### PROTECTING THE SOLDIERS' HEALTH

THE effectiveness of modern preventive medicine in keeping down the incidence of disease is demonstrated by the general health of the Army in India.

T. A. B. inoculation with a new strain of organism included brought about a further fall in the military incidence of enteric fevers during 1938, whilst the relative absence of cases of smallpox and cholera among the troops in areas in which these diseases have been prevalent in epidemic form all go to illustrate what can be done by preventive medicine.

Thus, there has been a general reduction in the number of cases of malaria among the troops over the last ten years, the number of cases among British troops being less than one-half of what they were ten years ago, and the number of cases among Indian troops having dropped by more than one-third. There has also been a marked drop in the number of relapses.

Perusal of the clinical records of the cases placed on the dangerously ill list and of cases of outstanding interest disclose that the standard of professional ability displayed by medical officers and nursing staffs of hospitals is of a high order. It also helps one to realize that to-day the combined resources of the medical services of the Army in India place at the disposal of the soldier and his family and the sepoy and his family (for the latter the work is only now commencing) a proficiency in treatment and care equal, bearing in mind the physical standard of the population, and the incidence of diseases to which they are liable, to the voluntary hospital in the United Kingdom and only at the call of the wealthy in civil life.

#### FOUR YEARS' SUPPLIES OF QUININE PURCHASED

THE Government of India have taken steps to ensure that there shall be an adequate supply of quinine sulphate in India for all purposes for which Provincial and State Governments normally require it. Provision has also been made for the estimated requirements of the defence services.

Statistics were collected showing probable requirements over a period of years. The amount involved being substantial, the Government of India approached the authorities in the Netherlands East Indies and an agreement has now been concluded by which practically the whole amount required over the next four years will be shipped from Java during the next six months. Owing to the size of the contract it has been possible to arrange considerably reduced terms.

## Current Topics

### The Diagnosis and Treatment of Syphilis of the Nervous System

By FERGUS R. FERGUSON, M.D., D.P.H., F.R.C.P.

(From the *Practitioner*, Vol. CXLIV, April 1940, p. 354)

OWING to the fact that syphilis may attack any portion of the central nervous system—meninges, arteries or the nerve elements themselves—the clinical manifestations are legion and, if mistakes are to be avoided, it is clear that the possibility of syphilis being the causative agent must be borne in mind in practically every patient with a nervous disease in which there is uncertainty in diagnosis. This applies whether the history is short or of ten to twenty years' duration, whether the principal abnormality is a psychological one or whether the problem consists of isolated or multiple cranial nerve palsies, of a hemiplegia or paraplegia, or of such widely different symptoms and signs as impotence and incontinence, arthropathies and ataxia, paræsthesia or ptosis, dysarthria or dementia, diplopia or dyspnoea, deafness or depression.

#### TYPES AND CLASSIFICATION

The diagnosis of neurosyphilis includes first the differentiation from other neurological conditions, such as cerebral tumour, disseminated sclerosis, subacute combined degeneration of the cord, progressive muscular atrophy, spinal tumour, and so on, and secondly, the

diagnosis of the particular type of neurosyphilis, i.e., whether tabes dorsalis, Erb's syphilitic spinal paralysis, general paralysis of the insane (G. P. I.), or gummatous basal meningitis.

It has for years been customary to accept the essentially different pathological forms of neurosyphilis—parenchymatous, in which the underlying lesion is in the nerve elements, and primary meningo-vascular syphilis, in which the initial lesion is in the blood vessels or meninges. The changes in the cerebro-spinal fluid and the morbid anatomical findings suggest that such a distinction is most probably unjustifiable and incorrect, and most observers now hold the view that the vessels and meninges are primarily affected in all forms of neurosyphilis, and that parenchymatous syphilis as an initial lesion does not exist. Further, although it is true to say that clinically typical examples of tabes dorsalis and G. P. I. are often encountered, yet only too frequently patients are found to present some of the classical features of, say, tabes, but have in addition vascular or meningitic manifestations. There is much overlapping, and considerable difficulty may be experienced in placing a particular patient in one of the recognized groups. Thus a sharp distinction between the various types of neurosyphilis is often impossible and there are those who advocate that on clinical and pathological grounds classification should be restricted to syphilitic meningitis, encephalitis, myelitis and encephalomyelitis. Such a simple subdivision has its attractions but, in the present state of knowledge, more elaborate classification must be

retained. In the course of practice the following has been found useful:—

**Congenital:** G. P. I., taboparesis, tabes and a heterogeneous group including hydrocephalus, meningitis, mental defect, cranial nerve paralysis, epilepsy, paralysis of the extremities, and the 'nervous child'.

Acquired	Meningo-vascular	Parenchymatous
<b>Brain—</b>		
Cerebral syphilis	Pachymeningitis Gummatous leptomeningitis.	G. P. I.
<b>Spinal cord—</b>		
Spinal syphilis	Gummatous Cerebral thrombosis Pachymeningitis Meningomyelitis Erb's syphilitic spinal paralysis. Spinal thrombosis Radiculitis Caries	Tabes dorsalis.
<b>Brain and spinal cord.</b>	Cerebro-spinal syphilis	Taboparesis.

#### DIAGNOSIS

In view of the wide range of signs and symptoms caused and clinical pictures presented by these various types of neurosyphilis it is not possible, in this article, to give a full or adequate differentiation from the large number of nervous diseases with which they may be confused. It is proposed to enumerate some of the presenting signs and symptoms of neurosyphilis, and some of the commoner conditions which may give rise to similar symptoms, and which have given rise to difficulty in diagnosis.

**Headache.**—Cerebral tumour, sinus disease, cerebro-vascular disease, meningitis.

**Diplopia.**—Disseminated sclerosis, myasthenia gravis, cerebral aneurysm, encephalitis.

**Optic atrophy.**—Toxic amblyopia, disseminated sclerosis, pituitary tumour, intracranial meningioma, cerebral aneurysm, chiasmal arachnoiditis.

**Facial pain.**—Trigeminal neuralgia.

**Lightning pains.**—Rheumatism, fibrositis, arthritis, peripheral neuritis, subacute combined degeneration of the cord.

**Trunk hyperæsthesia.**—Psychoneurosis, neuritis, radiculitis, spinal tumour.

**Atrophy of hand muscles.**—Progressive muscular atrophy (amyotrophic lateral sclerosis), syringomyelia, spinal tumour.

**Charcot joints.**—Syringomyelia, arthritis.

**Disturbances of micturition.**—Prostatic or bladder diseases, cauda equina tumour.

**Impotence.**—Disseminated sclerosis, cauda equina tumour, hysteria, endocrine lesions, and general ill health.

**Perforating ulcers.**—Spina bifida, diabetic neuritis, peroneal muscular atrophy.

**Spastic paraplegia.**—Disseminated sclerosis, spinal neoplasm, subacute combined degeneration of the cord, amyotrophic lateral sclerosis, syringomyelia.

**Rombergism.**—Peripheral neuritis, subacute combined degeneration of the cord.

**Epilepsy.**—Cerebral tumour, cerebro-vascular disease, idiopathic.

**Gastric crises.**—Ulceration or perforation of the stomach or duodenum, acute cholecystitis.

**Absent tendon reflexes.**—Myopathies, progressive muscular atrophy, subacute combined degeneration of the cord, Friedreich's ataxia, myotonic pupil (Holmes-Adie syndrome). It is very important to recognize and differentiate this last condition from tabes dorsalis because there is no evidence that it is progressive and, although the ætiology is obscure, yet it is clearly not

syphilitic. The syndrome is characterized in its complete form (a) by pupils (or a pupil, for the pupillary phenomena are often unilateral) which show little or no reaction to light and slow convergence and still slower dilatation on relaxation, and (b) by the absence of some or all of the tendon reflexes.

It is hoped that this emphasis on, and presentation of, the principal or initial symptoms, rather than the 'full blown' disease and its clinical picture, may lead in a doubtful case to a suspicion of a syphilitic cause for the symptoms, to a search for syphilitic abnormalities, e.g., in the pupils, iris, or heart; to examination of the blood and cerebro-spinal fluid; to a careful history and, in turn, to earlier and more successful treatment.

Although from the clinical description the differentiation between tabes dorsalis and peripheral neuritis should be fairly easy yet in practice it is found that this problem is at times a difficult one. It is true that the patient may have courted both diseases, but it is more than probable that one or the other is giving rise to the incapacity. Important differentiating points are the presence or absence of deep tenderness and the type of sensory loss but, even after the examination of the blood and cerebro-spinal fluid, we may be dependent on the results of therapy for the correct diagnosis.

The recognition of G. P. I. is not generally difficult if the disease is borne in mind, especially when confronted with the problems of epilepsy starting in adult life, speech defects, obscure and generalized tremulousness and psychological changes—defective memory for recent events, confusion or periods of excitement. The condition is generally labelled neurasthenia, but the other diseases with which it has been confused include frontal tumour, cerebro-vascular disease, presenile dementia, Huntington's chorea, chronic alcoholism, and barbiturate intoxication, which may give rise to confusion, slurred speech, fixed pupils, ocular palsies, ataxia and facial tremor.

#### WASSERMANN AND CEREbro-SPINAL FLUID

Although neurosyphilis and its particular type may be capable of recognition on clinical grounds, yet two of the most valuable aids are the Wassermann reaction—and allied tests—and complete examination of the cerebro-spinal fluid. In this connection there are several important points which must be borne in mind:—

(1) In *tabes dorsalis* the Wassermann reaction is positive in both blood and cerebro-spinal fluid in 65 per cent of cases, positive in the fluid alone in 10 per cent, in the blood alone in 5 per cent, and *negative in both* in 20 per cent. The percentage of positives and negatives will differ in different series, but nearly all observers agree that the blood Wassermann is negative in at least 30 per cent of cases. It is important to stress this fact, for there are many practitioners who still doubt its truth. It is reported that if 1 c.cm. of cerebro-spinal fluid is used instead of the original amount—0.2 c.cm.—the Wassermann in the cerebro-spinal fluid will generally be positive, but on this there is no unanimity of opinion. In *tabes dorsalis* there is often an excess of cells and, in 90 per cent of cases, there is excess of globulin, but a negative blood and completely normal fluid may be found not only in the long standing ataxic and so-called 'burnt out' cases, but also occasionally when the disease is progressive.

(2) In contrast to this the Wassermann is positive in the blood in practically 100 per cent of cases of G. P. I. In clinical practice it is fortunate that it is thus possible to make or confirm the diagnosis without a cerebro-spinal fluid examination.

(3) In early *meningo-vascular syphilis* the blood is usually positive, but it may be negative if efficient treatment has only recently been given. Therefore examination of the cerebro-spinal fluid is essential in doubtful cases, when the blood is negative.

(4) The finding of a paretic or 'first zone' gold curve does not necessarily mean *neurosyphilis*, in fact when it is combined with a negative Wassermann the cause is generally disseminated sclerosis.

(5) There is considerable variation in the effect of treatment on the abnormalities in the cerebro-spinal fluid. At times the clinical and serological improvements occur *pari passu*, but symptomatic cures may be obtained without change in the cerebro-spinal fluid and, conversely, the fluid may revert to normal while the clinical symptoms continue to progress.

(6) The fluid changes in dementia paralytica and tabes dorsalis are usually the most difficult, and those in acute syphilitic meningitis or vascular neurosyphilis the easiest to influence.

It is important to remember that although serological tests are so valuable in the diagnosis of neurosyphilis, still on occasion the Wassermann reaction is found to be positive, and yet a non-syphilitic lesion has proved to be the cause of the symptoms. In a series of cases from the National Hospital, London, on four occasions the Wassermann was positive and yet a non-syphilitic spinal tumour was removed.

I have also seen typical chronic encephalitic Parkinsonism and lead myopathy as the cause of the incapacitating symptoms when the Wassermann reaction was positive in the blood.

Occasionally two conditions may be present.

A patient recently under my care had subacute combined degeneration of the cord with achlorhydria and a pernicious anaemia count and, in addition, showed signs of tabes dorsalis with a positive Wassermann and typical changes in the cerebro-spinal fluid.

Further, although abdominal pain and vomiting in tabes dorsalis may be due to gastric crises, other causes must be excluded. A gastric ulcer has been found to be the cause of such symptoms and it has healed with appropriate treatment. It is clear therefore that, even although the Wassermann is positive, a careful clinical examination and further investigations must be made in order to exclude any other cause for the symptoms. It is especially important to remember this because the recent tendency, when the Wassermann reaction is found to be positive, has unfortunately been to start immediately on a course of anti-syphilitic treatment and to omit a detailed neurological and general examination.

#### TREATMENT

The treatment of *neurosyphilis* may be considered under four headings—(1) General. (2) Symptomatic. (3) Anti-syphilitic. (4) Thermo-therapy.

The tendency just referred to, to omit or curtail a general examination, is also reflected in therapy; neglect of the general and symptomatic treatment is frequently found. Neurosyphilitic therapy is frequently controlled by and carried out—in some centres almost entirely—in V. D. clinics. The great advantage of this is that, owing to the excellent general organization of such clinics, the anti-syphilitic treatment is thorough and well supervised and the injections are efficiently and successfully given, so that it is not difficult to get the patient to continue with his treatment. On the other hand, it is hoped that this practice will not lead to neglect of a careful general examination, to the treatment of a *disease* rather than a patient, and to control of treatment by the blood and cerebro-spinal fluid rather than by the clinical state, for it is recognized how often the clinical and serological improvements do not go hand in hand.

**General.**—It is essential to keep the general health as good as possible—a regular life, avoiding all excesses, including sexual indulgence; abstinence from or at least extreme moderation in smoking and alcohol—and physical and mental exertion must never be pushed beyond the point of fatigue. The tabetic would be best advised to follow Erb's advice and live the life of an old man, simple, abstemious, quiet and regulated.

**Symptomatic.**—Attention to the bowels and bladder is extremely important but is often neglected in the treatment of a tabetic. Reference to these and other symptoms will be made in later paragraphs.

**Anti-syphilitic.**—It will not be possible to discuss in detail the merits of the numerous preparations, or the

advantages or disadvantages of all the different 'lines' of therapy. It is proposed to deal with general principles and aspects in therapy which receive too little attention or the undeservedly omitted. The preparations which are most commonly used are iodides, bismuth or mercury and arsenic. First, a brief note about these preparations—

**Iodides**, which some years ago were always used, are now at times almost forgotten or at any rate are given somewhat perfunctorily and in inadequate doses.

**Mercury** has been condemned by some authorities as harmful. Others deny this and attribute the ineffective results to inadequate administration, and regard it as one of the most valuable weapons in the anti-neuro-syphilitic armamentarium. Mercury may be given as liq. hydrarg. perchlor. or pil. hydrarg. et iod. virid., but one of the most useful methods is by inunction. This, however, must be done efficiently—preferably by a professional rubber—and the ointment must be rubbed in for fifteen to thirty minutes and the course continued until signs of mercurialism are produced.

**Bismuth** is at present fairly widely used because it frequently gives excellent results, often better than with mercury, but it is difficult to predict in which type of neurosyphilis, and in which particular case, it will be of the greatest value.

**Arsenic** is the metal most commonly and constantly employed and in general is regarded as being of the greatest value. In the opinion of many tryparsamide—a pentavalent arsenical—is of more value than the more commonly employed trivalent arsenicals, especially in tabes and G. P. I. Its principal disadvantage is its liability to cause optic atrophy and, further, it has apparently little effect on syphilitic lesions other than those in the nervous system. Before tryparsamide is given, the fundi must be examined and the fields of vision charted. Any reduction or alteration in the fields should be a sign to stop the administration.

Secondly, should faith be pinned in a particular case to one or at the most two of the preparations or should all four be given?

Thirdly, it must be decided whether the preparations should be given concurrently in order to obtain a maximal or synergic effect, or consecutively. Two points in favour of the latter method are that it frequently affords a better idea of which substance is the most valuable and gives the greatest clinical improvement in a particular case. Secondly, nausea, loss of appetite and general malaise may follow the combined use of iodides, mercury and N. A. B., and yet when the iodides and mercury are omitted the patient may be able to tolerate full doses of arsenic. Although entering the therapeutic arena some years ago with a flourish of trumpets, intrathecal injections of salvarsanized serum have no especial advantage, according to most observers. There is still much difference of opinion as to the relative value of, and the special indications for, these preparations. Each has its own advocates and the virtues of one preparation are often extolled to the exclusion of the others. It is little wonder then that a practitioner, who may encounter a new case of neurosyphilis only once a year, finds himself in confusion and without a definite plan of action, and in consequence the therapy and the patient suffer.

Although many are accustomed to prescribe different lines of treatment for the different neurosyphilitic syndromes, yet in view of the probable basic common pathological process, the coincidental presence of syphilitic lesions elsewhere, the overlapping of the clinical pictures and the difficulties and uncertain nature of our classification, it is difficult to defend and find justification for widely dissimilar methods of treatment. In the present state of knowledge with some uncertainty about the pathology and the need for adopting a modified clinical classification, variations in therapy must be allowed in some degree, but for practical purposes there should be a basic course of anti-neurosyphilitic treatment which can be adopted when the exact designation of a particular case is uncertain.

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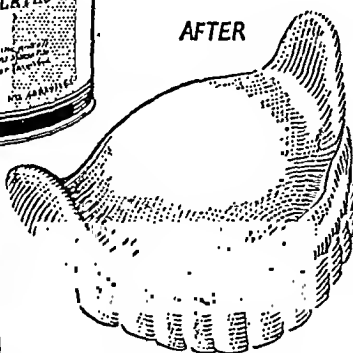
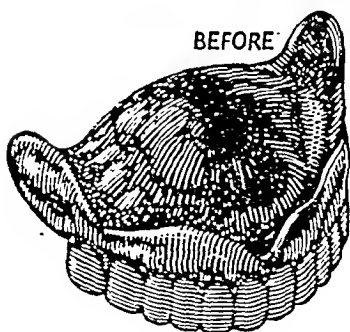
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- (1) Pot. iod. 10 grains three times daily for two weeks.
- Pot. iod. 15 grains three times daily for the following two weeks.
- Pot. iod. 20 grains three times daily for the succeeding two weeks.

(2) At the same time give two courses of mercurial injections:—Ung. hydrarg. (B.P.) 60 grains to be well rubbed in daily—on successive days into an arm, leg, or the trunk. A course to consist of twenty injections and the patient to have a week's interval between the two courses.

(3) After an interval of a week to start a course of novarsenobillon or stabularsan, or one of the trivalent arsenicals: eight weekly intravenous injections, starting with 0.3 gm., then 0.45 gm., and then six injections of 0.6 gm., with a total of 4 to 5 gm.

(4) After two weeks' interval follow with a course of bismuth—2 c.cm. or 3 grains twice weekly intramuscularly for twelve injections.

This course of treatment will take approximately six months and, unless there are contra-indications, it should be followed by two similar courses during the next two years and then one course yearly for the succeeding three years. If it is desired for practical reasons to shorten the course to four months then half the arsenic therapy may be given during the second month and the second half along with the bismuth during the third month. These courses may seem rather long and drawn out but the majority of the cases are not urgent and do not require initial drastic therapy.

I often think that we make our metallic onslaught in neurosyphilis too heavy and then rather tend to fall away, if immediate results are not produced. If we made a more gentle attack then I am sure both we and our patients would benefit. If one of the preparations gives adverse reactions, then this should be omitted from future courses. *It is extremely important to stress the fact that continuation of the treatment must be dependent on the clinical improvement of the patient.* There is no use continuing with anti-syphilitic treatment if there is no clinical improvement during the second course of treatment. It is clear therefore that we must be prepared to modify the dosage, the intensity of the treatment, the frequency and number of courses, and to discuss additional treatment—such as induced pyrexia—to meet the needs of special cases, and to vary the course when it is clear that the maximal incidence has been on the meningeal or vascular tissues or on the parenchyma.

#### SPECIAL CONSIDERATIONS IN TREATMENT

**Meningo-vascular.**—When it is not possible from the clinical symptoms and signs to decide whether the meninges or the vessels are more affected, then the above course should be given. When, however, the meninges are principally involved, then the arsenic injections may be started after the first fortnight or month and given concurrently with the iodides and the mercurial injections. In acute syphilitic meningitis the arsenical therapy may be started at the end of the first week. In the vascular syphilitic lesions, however, it is wise to postpone the arsenic administration for the full two months and then when the arsenic is given to make the initial doses small and increase them gradually—0.15, 0.15, 0.3, 0.3, 0.3, 0.45, 0.45, 0.6 gm., because of the liability to Herxheimer reactions.

Although there is a general impression that the prognosis in neurosyphilis is quite good, and particularly so in meningo-vascular syphilis, and although it is true if the meninges alone are involved that the outlook is good, yet the results are only too often disappointing when there is arterial obstruction and when there have been softenings, hæmorrhages, or tract degenerations.

**Tabes dorsalis.**—The lack of response in long-standing tabetics with marked ataxia and loss of weight or optic atrophy is often striking, whereas the results

are encouraging in those with a shorter history. Therapeutically, if there is no response to the initial course then tryparsamide should be given a trial—intravenous weekly injections with an initial dose of 15 grains, then 20 grains for twelve injections, in two courses of six injections with one month's interval. If the tryparsamide does not produce improvement then the advisability of thermotherapy must be considered. Only too frequently, however, in the chronic tabetic it is necessary to rely on general and symptomatic treatment, and attention to both of these aspects may gain the gratitude of patients, although the symptoms are by no means readily responsive to treatment.

**Bowels.**—Similarly the bladder must be emptied regularly—the call to micturition must be by the clock—every three hours. If the tendency is to true incontinence of urine then help will often be obtained by tinct. belladonnæ, 5 minims three times a day, but if there is atony of the bladder, with difficulty in passing urine and retention, then liq. strych. 5 minims should be given three times a day. Although there is for many reasons a natural desire to postpone catheterization as long as possible yet, on the whole, when retention develops or if the bladder becomes palpable, it is wisest not to delay the measure. The urine must be examined regularly for pus cells, and if present a course of urotropine and acid. sod. phos. prescribed, or if not effective, bladder lavage. Careful attention to the bladder function is stressed, for the life of the tabetic is constantly menaced by the possibility of cystitis or ascending pyelonephritis.

**Ataxia.**—Despite increased knowledge of the early symptomatology of tabes, yet only too frequently the symptom which causes the patient to seek advice is unsteadiness in walking. This ataxia may be much improved by training the patient to make greater use of his remaining powers, by concentrating his attention on his movements and careful re-education walking exercises. It is certain, however, that unless there is real effort and constant supervision or, on the other hand, if the physiotherapy is perfunctory and the treatment by the clock and in a large class rather than as an individual, then the results will be disappointing.

**Gastric crises.**—These are often extremely troublesome and resistant to all forms of treatment. If the patient is able to retain anything by mouth chlorotone, 10 grains in a cachet, freshly prepared may be tried. If this dose is not successful and there is no resultant depression of the heart and respiration, then 20 grains may be tried. Other measures which may be helpful are tinct. belladonnæ, 10 or 20 minims, or alternatively, adrenaline hydrochlor. 1 in 1,000 or atropine sulphate, grain 1/1,000 by injection.

A useful prescription is:—

Sod. bicarb.	..	..	10 grains
Acid. hydrocyan. dil.	..	..	3 minims
Liq. adren.	..	..	5 minims
Syr.	..	..	q.s.
Aq. chloroform	..	..	ad. ½ ounce

When the symptoms are still severe and anti-syphilitic and symptomatic measures have failed, thermotherapy or chordotomy must be considered. If the crises still persist then morphine may have to be used but it should only be as a last resort, for the danger of addiction in gastric crises and in lightning pains is very real.

**Lightning pains.**—Similarly these often make both the patient and practitioner desperate and here again morphine should be avoided. Veramon, 6 to 12 grains, is one of the most useful preparations, but it is generally best to ring the changes on the analgesics. Two useful prescriptions for severe cases are:—

Phenacetin	..	..	10 grains
Aspirin	..	..	10 grains
Heroin hydrochlor.	..	..	1/6 grain. Fiat pulv.

(The patient must not know the composition.)

or Medinal	..	..	10 grains
Codeine	..	..	½ grain
Phenacetin	..	..	10 grains. Fiat pulv.

Intravenous hypertonic saline, a single dose of T. A. B. vaccine or injections of stabilarsan have been employed with success, but have failed in many cases. Attention must be paid to warmth, constipation, and abstinence, for these are valuable auxiliaries in the treatment of this distressing state.

Perforating ulcers may be dressed with a paste of iodine and starch, but the only adequate treatment is complete rest to the foot. The tabetic should not cut his corns.

#### DEMENTIA PARALYTICA: INDUCED PYREXIA

The methods employed in the treatment of G. P. I. are: (1) anti-syphilitic as outlined above; (2) induced pyrexia—(a) malarial, (b) chemical—as with sulphosin, (d) physical, or as is generally advocated; (3) a combination of anti-syphilitic measures and thermotherapy.

Wagner-Jauregg introduced malarial therapy for G. P. I., and for some years this has been the method of choice in this country, so that figures for ten years (1927–1937) are now available from the Ministry of Health. There is no doubt that some striking results and remissions have been obtained, and that in a number of cases the improvement has been maintained, but it is equally true that many feel that the present position is somewhat disappointing, that the numbers of 'cures' are not so large as were expected and that there is a serious growing problem of the 'half cured' general paralytic.

Some years ago it was thought that the favourable results obtained with malarial therapy were due largely to the specific action of the malarial organism. Most of the recent evidence goes to show, however, that there is no especial virtue in malaria as such and that the method of induced pyrexia, which most consistently produces a sustained fever, will be most successful. If this is correct then the rivalry is between the malarial and physical forms of therapy. In the latter field several different methods have been advocated. It is now ten years since Neymann and Osborne of Chicago (1929) employed diathermy; since then, short radio waves—the radiotherm, the inductotherm, the Kettering hypertherm (using hot humidified air), or the Honsaker machine (using hot water vapour) have been employed. In this country this method has not received sufficient general attention but a series of careful investigations and observations have been carried out for some years by Nattrass and Evans in Newcastle. Nattrass recently communicated their results to the Medical Society of London. They have obtained good results with a simple hospital-made radiant-heat cabinet. This method has the merit of low cost, and a continuous record of temperature can be kept by an electrical rectal thermometer. (This thermometer cannot be used continuously when high-frequency currents are employed.) Other advantages were that there was relatively little discomfort and the patients were not made ill—as with malaria. There was no anaemia and no jaundice, and the fever could be precisely controlled. The fever is continued until the maximal clinical response has been obtained—an average of four to six pyrexias of 106°F. each lasting eight hours. For safe and effective treatment the staff should be specially trained and the work carried out in a special department. This pyrexial treatment must be supplemented by specific therapy; tryparsamide and bismuth seem to be of especial value. This should be given not longer than a month after the course of the fever; in general, it has been found too dangerous to inject the preparations at the height of the fever.

In comparing different methods of treatment in G. P. I. there is the difficulty that the groups of patients under review are often considerably different—the one in a mental hospital, and the other in private practice or attending a general hospital. The great disadvantage to malarial therapy is its mortality. Although the figures differ considerably, yet in most hands it is between 10 to 15 per cent. It seems clear that the mortality is lower when physical means are employed, and Nattrass reported that during the past

four years 213 patients with G. P. I. have been treated without a death.

The best results which I have seen in dementia paralytica have been obtained by giving the 'initial' course as outlined, followed by malarial therapy and then, after a three months' interval, by a course of six tryparsamide treatments given in the following manner:—

(1) A lumbar puncture is performed and the cerebro-spinal fluid is drained off.

(2) Then 30 c.cm. of hypertonic saline are given intravenously.

(3) After half to one hour the tryparsamide is given intravenously.

Hinsie and Blalock show that of the three methods—tryparsamide alone, malaria and tryparsamide, and electro-pyrexia and tryparsamide—the best results, clinically and serologically were obtained by the last combination. It is difficult therefore to decide at the present time which form of therapy to adopt in G. P. I. On the whole in a case of average severity and in which there is no especial urgency, I would suggest starting with the initial course—beginning the arsenical administration after the first two weeks whilst arrangements are being made for electro-pyrexia if available, or otherwise for malarial therapy, for in view of the mortality rate it is essential to discuss the position carefully with the relatives. Then as soon as possible—within a month of the physical pyrexia, and within three to six months after malaria—a course of tryparsamide and bismuth should be given.

It is still too early to be dogmatic about the relative merits of electro-pyrexia and malaria, but the evidence brought forward by Nattrass and Evans suggests that the former is the more effective and much safer. The methods of physical pyrexia require some co-operation on the part of the patient and therefore, in some cases, malaria must still be the method of choice. There are many who advocate that as soon as evidence is available by a cerebro-spinal fluid examination or clinical signs or symptoms that the nervous system is involved then pyrexial treatment should be instituted without delay. Had it not been for its associated mortality, malaria might already have been employed more generally and in the earlier stages. If Nattrass and Evans are able to continue to show that with care their method has no mortality, then it may well be that in five years' time, the routine treatment for neurosyphilis will be with electro-pyrexia, and one or more of the anti-syphilitic preparations.

## Reviews

**VIRUS DISEASES OF MAN.**—By C. E. van Rooyen, M.D. (Edn.), and A. J. Rhodes, M.B., Ch.B. (Edn.), M.R.C.P.E. 1940. Oxford University Press, London, Humphrey Milford. Pp. xxxv plus 932. Illustrated. Price, 65s. Obtainable from Oxford University Press, Bombay and Calcutta

THE immense amount of work that has been done on viruses and the discovery of many new ones in the last twenty or thirty years is indicated by the fact that it now needs a volume of 900 pages adequately to deal with those viruses which affect man only. Such a book is the one under review, and it is a product of the Department of Bacteriology of the University of Edinburgh.

The book opens with an interesting and instructive summary on viruses in general by Prof. T. J. Mackie and includes a discussion of the modern views on the probable nature of these bodies. This introduction ends with a list of thirty diseases of man definitely proved to be of virus origin. Others in which the aetiological connexion of viruses is strongly suspected, but is not yet proven, are not included in the book.



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This book can accordingly be described as a valuable compendium on the subject of virus diseases of man as it contains sufficient practical information on which to commence the study of viruses in the laboratory; it describes in adequate detail the different diseases caused by viruses giving historical facts when these are of interest and value, and it contains in its numerous lists of up-to-date references an exhaustive guide to wider reading on any special aspect of the subject. It can be recommended with confidence as a most valuable book for the acquisition of knowledge on any branch of virus disease in man.

It is plainly and strongly bound and is a credit to the authors and publishers.

P A M

**CLINICAL METHODS: A GUIDE TO THE PRACTICAL STUDY OF MEDICINE.**—By Sir Robert Hutchison, Bart., M.D., LL.D., F.R.C.P., and Donald Hunter, M.D., F.R.C.P. Eleventh Edition. 1940. Cassell and Company, Limited, London (La Belle Sauvage, E.C.4). Pp. xiii plus 622. Illustrated. Price, 13s. 6d.

The reviewer first learnt to value this book as an inseparable companion during his hospital work as a student; it was then in its third edition. Apart from the fund of information it contains one of its greatest claims to popularity is its convenient size so that it can be taken into the wards and clinical laboratories, and in spite of the numerous additions to clinical methods of investigation that are constantly being made this small volume is no larger than it used to be. To maintain their usefulness without increasing their size is an achievement which few of the regularly appearing medical books can claim. There are now many other publications of a similar nature to 'Clinical Methods' but none with which the reviewer is acquainted are its equal in value, and he feels he cannot give better advice to the student just beginning his hospital studies than to tell him that whatever calls there may be on his budget, the expenditure of the modest sum of thirteen shillings and sixpence needed to acquire this book is likely to prove one of the best investments of his student career.

**OBSTETRICS AND GYNÆCOLOGY.**—By Departmental Staff of the University of Chicago and other Contributors. Edited by F. L. Adair, M.A., M.D., F.A.C.S. Volumes I and II. 1940. Henry Kimpton, London. Pp. 1000 in volume I. Illustrated with 359 engravings and 14 plates. Pp. 1031 in volume II. Illustrated with 304 engravings and 10 plates. Price, £5-0-0.

This great work edited by Dr. Adair is the result of the combined efforts of 63 contributors and collaborators. No names, however, are associated with individual chapters or sections and it is indicated that such individual chapters may not always be the work of one contributor, but frequently the result of the efforts of a group.

By far the greater part of the two volumes is taken up with obstetrics in fact gynecology is considered as being of secondary importance.

The fact that several authors have taken part in the production of this work, of necessity makes for some re-duplication of descriptions, this however in no way detracts from its merit.

The general arrangement is somewhat different from that which is usual in most textbooks, in that a chapter on a gynecological complaint may be found between two chapters on obstetrical conditions. This

is a little surprising, but if the work be read as a series of articles in continuity, any difficulty will disappear.

A great amount of space is taken up with treatises on the correlation of the anatomy and physiology of the mother and foetus, the biology of human reproduction, and embryology. There are also extensive chapters on the effect of pre-existing disease on pregnancy. Heart disease and tuberculosis being especially well described, and excellent advice given.

All the above is very interesting reading and a change from the too-often-bald descriptions of many of the textbooks.

The volumes record the thought and teaching of the Chicago School based on the experience of many years.

While the Chicago School is dogmatic, and quite rightly so, in insisting on rigid attention to detail in every respect, it is extremely tolerant of the methods of other schools, and in its treatment combines many methods of proved value. As for instance in eclampsia, a method of treatment combining that of Stroganoff with venesection, and the Dublin School is the choice.

The Watkins operation for the cure of backward displacement of the uterus is advocated. This however is not popular with European gynecologists.

The appendices contain diet and other charts, food values, and quite a long dissertation on clinical pathology and bacteriology, and nursing.

The two volumes are a monument to a great effort which is meant to be a textbook. Thus it undoubtedly is, but there is a great deal more to it than a simple textbook.

H E M

**GREEN'S MANUAL OF PATHOLOGY.**—Revised and Enlarged by H. W. C. Vines, M.A., M.D. Sixteenth Edition. 1940. Baillière, Tindall and Cox, London. Pp. viii plus 1166, with 701 illustrations. Price, 31s. 6d.

This has been one of the standard textbooks on pathology for several generations of medical students in many parts of the British Empire.

It is stated in the preface that this edition has been somewhat enlarged and one of the reasons given for this change is to try and make it less academic than its predecessors. One of the changes is the omission of chapters on pure bacteriology and pure parasitology, 'as they should be studied in appropriate textbooks'. We wholly agree with this point of view, but consider that having left out these chapters it would have been better to have omitted the subjects altogether and referred readers to appropriate books on them, than to have given the totally inadequate and consequently often misleading statements that have been included. Let us take some random examples from the few pages devoted to animal parasites. The only intestinal protozoa mentioned are *Entamoeba coli* and *E. histolytica*, hookworm disease or, as it is now almost universally called, 'ankylostomiasis', is found under the out-of-date and strictly speaking incorrect name of 'Uncinariasis', and of flukes we are told, 'The only species commonly parasitic in man are *Distoma pulmonale* which is the cause of Asiatic distomiasis and the *Schistosomum hæmatobium* or *Bilharzia hæmatobia*'. These should suffice to support the reviewer's contention.

Another section of particular importance to students in the tropics are the anæmias, and this portion of the book is very disappointing as there is no attempt at a comprehensive up-to-date classification of these blood diseases nor is the modern nomenclature made use of to any extent.

Other sections, dealing with tissue changes in various diseases and the tumours which occupy the bulk of the book, are as good as they always have been and it is with real regret that the reviewer feels compelled to criticize so severely an old friend of his student days for serious shortcomings in certain small sections, but he has reviewed the book from the point of view of the student in the tropics and feels he cannot recommend it from this particular aspect.



**STANDARD METHODS OF THE DIVISION OF LABORATORIES AND RESEARCH OF THE NEW YORK STATE DEPARTMENT OF HEALTH.**—By Augustus B. Wadsworth, M.D. Second Edition. 1939. Baillière, Tindall and Cox, London. Pp. xxiv plus 681. Illustrated with 39 plates and 55 figures. Price, 41s.

THE issue of the second edition of this well-known book on standard methods will be welcomed by all who are familiar with the first edition published in 1927 and which soon established a reputation as a standard work on laboratory technique. Those who have had many occasions to refer to it for guidance and instruction will find the second edition even more valuable than its predecessor. A considerable amount of revision has been made and by segregating in one section—'on general laboratory procedures' the technical details of methods common to different branches of the work, the author has succeeded in including important new material without increasing the size of the book—in fact the new edition is a few pages smaller than the first. This in our opinion is a distinct advantage and avoids a considerable amount of repetition of technical details, and has resulted in a much clearer description, which gives to a better understanding of the different procedures.

Although there are available many books on technical methods there is not one quite like this one, not one that contains so much information, not one which will be referred to quite so often by laboratory workers engaged in routine work in clinical laboratories, or in research work or in the preparation of sera and vaccines on a commercial scale. Administrators of laboratory service will find in this book much that will be of great help in planning laboratory procedures to suit their particular needs. This is a book that should be in the hands of every bacteriologist for it is certain that it will be constantly referred to and be of inestimable help. It is both a 'desk and a bench book'.

C. L. P.

**ACUTE INFECTIOUS DISEASES: A HANDBOOK FOR PRACTITIONERS AND STUDENTS.**—By J. D. Rolleston, M.A., M.D. (Oxon.), F.R.C.P. (Lond.), F.S.A., and G. W. Ronaldson, M.D. (Glas.), D.P.H. (Oxon.). Third Edition. 1940. William Heinemann (Medical Books), Limited, London. Pp. ix plus 477. Price, 17s. 6d.

THE third edition of this book has been revised and enlarged, the main additions being chapters on erysipelas and isolation methods. There are no illustrations as the senior author considers that 'the only satisfactory place to study the cutaneous lesions of the acute exanthemata... is at the bedside'. No doubt this is the correct attitude to adopt for students, but many doctors like to refresh their memories before going to the bedside.

Full descriptions of the acute infectious diseases commonly seen in Britain are to be found in this book, including a very small chapter on the fourth disease.

The chapters on typhoid and paratyphoid fevers are of particular interest to practitioners in India and are exceedingly informative. The chapter on typhus deals with the classical, louse type only and for that reason is of limited value to those who deal with this somewhat complex group of fevers in the tropics.

Tropical infectious diseases such as cholera and plague are not included.

The book is written in a very pleasant and interesting way, and one can readily find all the information one requires. The treatment advocated is up to date and yet conservative.

It is one of the best books of its size on the subject of infectious diseases and as such can be thoroughly recommended.

J. G.

**LANDMARKS AND SURFACE MARKINGS OF THE HUMAN BODY.**—By L. Bathe Rawling, M.B., B.Ch. (Cantab.), F.R.C.S. Eighth Edition (New Terminology). 1940. H. K. Lewis and Company, Limited, London. Pp. viii plus 98, with 36 illustrations. Price, 8s. 6d.

THE first edition of this book appeared in 1904 and since then it has been the accepted guide of each successive generation of medical students. The new edition is sure to receive a great welcome from past and present students alike. The author's adoption of the British Revision of B. N. A. Terminology, now generally in use, will meet with approval.

In the past this book was chiefly used by the young surgical dresser but, under the new regulations of the Calcutta University, it will be found to be of great use to the pre-clinical anatomy class. The printing, binding and illustrations are all excellent.

P. N. R.

**INJECTION TREATMENT OF HERNIA, HYDROCELE, GANGLION, HÆMORRHOIDS, PROSTATE GLAND, ANGIOMA, VARICOCELE, VARICOSE VEINS, BURSAE AND JOINTS.**—By P. Riddle, B.S., M.D., F.A.C.S. 1940. W. B. Saunders Company, London. Pp. ix plus 290, with 153 illustrations. Price, 27s. 6d.

INJECTION therapy is rapidly approaching a status which may confer upon it the dignity of a special subject. It is, however, necessary to emphasize that this method is not applicable in all cases and that in certain special cases it will not give as good results as surgery. The author has made an attempt here to include all those conditions to which injection therapy is applicable. This may be seen from the long list which is appended to the title of the book.

There are four parts in this book and at the end of each part there is an extensive bibliography. The first two parts deal with the injection treatment of hernia and varicose veins respectively, with adequate discussion of pathology, ætiology, complications and contraindications. In the third part there is a very good treatise on hæmorrhoids. The last chapter of part three, on the varicose theory of anal fissure, fistula and pruritus, will be found instructive. The final part is devoted to the consideration of an interesting medley including such subjects as hydrocele, varicocele, bursæ and joints, and the prostate gland.

We have no doubt that this book will be of use to the general medical practitioner and also to the general surgeon. The printing, get-up and illustrations are all very good but the price (27s. 6d.) will place the book out of reach of the man of moderate means.

P. N. R.

**ENDOCRINE GYNÆCOLOGY.**—Edited by E. C. Hamblen, B.S., M.D., F.A.C.S. 1939. Baillière, Tindall and Cox, London. Pp. xxviii plus 453. Illustrated. Price, £1 10s.

THIS book of 453 pages is concerned with the isolation and the synthetic preparation of endocrine glands, together with their therapeutic uses.

It is true that much of the subject-matter of the book has already appeared in various journals.

Dr. Hamblen has however collected and tabulated all this information into one volume, so that the reader may be enabled to find all information sought for, without having to search through various monographs.

There are numerous charts and graphs illustrative of the text.

The author must be congratulated upon the exhaustive study he has made into the early history and literature relative to the discovery of each of the endocrines and hormones.

The bibliography is very extensive and thorough. The book is well printed, and contains several good plates and many excellent photomicrographs.

H. E. M.



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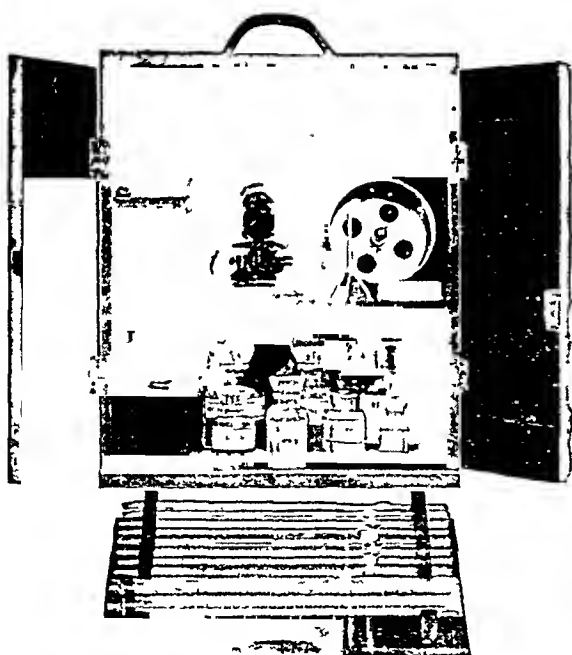
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**PHYSICAL TREATMENT BY MOVEMENT, MANIPULATION AND MASSAGE.**—By J. B. Mennell, M.A., M.D., B.C. (Cantab.), etc. Fourth Edition. 1940. J. and A. Churchill, Limited, London. Pp. xiv plus 669, with 281 illustrations including 32 plates, 8 in colour. Price, 25s.

Physical treatment in recent years has progressed in great strides owing to new additions to our knowledge of the physiology and biochemistry of living tissue. The first edition of this book was published in 1917, during the last Great War, but it was not intended to serve as a textbook for the massage student. The author's principal object was to place in the hands of his professional brethren a book to which they could refer when issuing instructions to their masseurs. The present edition fulfils the same object in greater measure.

There are altogether 32 chapters comprising 653 pages of reading matter, and the book deals with every condition for which physical treatment is indicated. Few will disagree with the statement that 'the masseur is born and not made'. Much has been written on the personal attributes desirable in those who undertake massage work; perhaps the first is that they should have suffered illness or injury themselves and have undergone a course of treatment. One eminent physician once said that he frequently ordered physical treatment to be carried out by a blind masseur but that if any one would introduce him to a dumb masseuse he would employ her all the time. It is the old story that 'the tongue is a smaller member but it is capable of inflicting unlimited harm'. So is tact a small word, but may well be the greatest asset to the masseuse. 'A smiling face oft masks a breaking heart' in the masseuse, but if it does so the patient should never be conscious of it. The choice of the masseuse, therefore, is of great importance in physical treatment. The chapters on medical gymnastics will be read with pleasure and profit, and those on backache are worthy of careful attention.

This book on physical treatment, now in its fourth edition, speaks for itself. We have much pleasure in recommending it to our colleagues. It will be useful to members of all branches of the medical profession. The printing and illustrations are of high quality and there is a useful index.

P. N. R.

**SURGERY OF THE HAND.**—By Marc Iselin, M.D. Translated by T. M. J. d'Offay, M.B., Ch.B. (Edn.), F.R.C.S. (Eng.), and T. B. Mouat, M.D., Ch.M. (Edn.), F.R.C.S. (Eng.). 1940. J. and A. Churchill, Limited, London. Pp. xiv plus 353, with 135 illustrations including 8 plates. Price, 21s.

This is a valuable monograph on wounds, infections and closed traumata of the hand by a well-known French surgeon. The translators deserve our best thanks for having made the book available to English-speaking people. In the author's preface to the English edition there is a poignant sentence which, in the light of recent history, makes tragic reading. 'The unhappy time of its publication prompts me to express the hope that it will help our British colleagues who are in the services to spend profitably those long hours of waiting that characterize this war.' It is dated March 1940, from the French Field Army.

This book consists of four parts, of which the first deals with wounds of the fingers and hand. The last chapter is devoted to the consideration of social problems arising out of such wounds. The author emphasizes the fact that the whole future of the patient is dependent on the first operation, which ought to be done as soon as possible. In part II there is a very instructive description of infections of the hand. The author does not exaggerate in stating 'that the great majority of complicated cases that we have had to treat have been incised elsewhere'. Closed traumata of hands and fingers are discussed in part III. The author's aphorism that 'the examination of closed

traumata of the hand and fingers is a radiographic examination' is worthy of note. The last part consisting of only six pages is a very important section, dealing as it does with assessment of incapacity.

This book has been described as a book for the practitioner and the surgeon. We strongly recommend it to our colleagues, who will certainly find it very useful in their everyday practice. The printing and illustrations are excellent, and a useful index is appended.

P. N. R.

**PROTOZOOLOGY.**—By Richard R. Kudo, D.Sc. (Enlarged and Completely Re-written Edition of 'Handbook of Protozoology'.) 1939. Baillière, Tindall and Cox, London. Pp. xi plus 689, with 291 illustrations. Price, 36s.

THIS is a book which deals with protozoology as a whole with the result that the comparatively few protozoa of interest to medical men and veterinarians tend to be rather submerged in a mass of protozoa of no medical or veterinary interest.

The book is only a handbook, so the descriptions of the various parasites are very short on account of limitations of space, and on this account the descriptions of the haemosporidia and trypanosoma pathogenic to man and animals are much too meagre for a medical man who has to deal with these parasites. One thing we were pleased to note, is the distinction between the genera *Entamoeba* and *Endamoeba* is recognized, a distinction not usually found in books of American origin.

Although of undoubted value for those who are undertaking the study of protozoology as a whole, it is felt that this book will not be of as much use to medical and veterinary students as one of the many books available that are devoted solely to the protozoa of importance as parasites of man and his domestic stock.

**OUTLINE OF PHYSIOLOGY.**—By William R. Amberson, Ph.D., and Dietrich C. Smith, Ph.D. 1939. The Williams and Wilkins Company, Baltimore. Pp. vii plus 412, with 177 figures. Obtainable from Messrs. Baillière, Tindall and Cox, London. Price, 22s.

THIS little volume has been written for students as an introduction to the study of physiology. In the early chapters the authors have dealt briefly with the modern physical and chemical concepts which the students of physiology are required to know. These ideas have been presented in a lucid style and will be of benefit to beginners. The inclusion of historical facts has made study of the book very interesting. The subject-matter in all the different sections has been written in a simple manner and as far as possible controversial points have been omitted. Details which are unnecessary for beginners have also been avoided and only the broad outlines and basic principles have been dealt with. The section on nervous integration of physiological function deserves special mention. The schematic diagrams are very helpful. Here also the fundamental points only have been presented, making the subject easily intelligible to a beginner.

P. D.

**NOTTER AND FIRTH'S HYGIENE.**—Revised by L. C. Adam, M.B., B.S., and E. J. Boome, M.B., Ch.B., M.R.C.P., D.P.H., T.D. Tenth Edition. 1940. Longmans, Green and Company, Limited, London. Pp. x plus 518. Illustrated. Price, 12s. 6d.

THIS is the tenth edition of a textbook originally published in 1894, the ninth edition of which came out in 1921. Consequently, as a well-known work, 'Notter and Firth's Hygiene' deserves due attention. However, the presentation of the subject conforms so much to the now outmoded approach to public health as a social welfare field that little can be said to recommend the

book for use in countries foreign to that of its publication. The factual material is relatively comprehensive and modern but so much of it is irrelevant to the daily routine of a Health Officer himself, particularly in India, that the book cannot be recommended for this country. In fact, textbooks on Public

Health Engineering and Microbiology, which to-day constitute the essential of every Health Officer's work-library, present most of the material in a more effective manner than the summary constituting the bulk of this text.

J. B. G.

## Abstracts from Reports

### THE ROCKEFELLER FOUNDATION, NEW YORK: A REVIEW FOR 1939. BY RAYMOND B. FOSDICK, PRESIDENT OF THE FOUNDATION

THIS year, owing to the rapid and stupendous changes that the war has brought to the whole of Europe, it is not possible to give an adequate abstract of the work of the Rockefeller Foundation as it has been further so greatly interrupted and disorganized since the report was written that the greater part of the report as far as Europe is concerned is altogether out of date.

We accordingly give below a short section from this report which is a valuable essay on recent achievements in scientific advancement and the dark future ahead of the world should European civilization go under.

#### DIVIDED WE FALL

One occasionally hears the statement that the trend of intellectual leadership is westward across the Atlantic. In proof of the assertion specific fields are mentioned, such as neuro-surgery, astronomy, dentistry and perhaps orthopedics, in which America has won pre-eminent standing. But this argument overlooks the many fields in which leadership, certainly until the war began, was still in Europe and the many others in which genius and stimulation are as potent on one side of the ocean as on the other. In physiology, for example, it would be difficult to determine whether the leadership lies in Europe or in the United States. The same is true of anatomy and pathology. In fields like pharmacology, tropical medicine, ophthalmology, legal medicine, social medicine and dermatology—to mention only a few—leadership is unquestionably still in Europe, or was in 1939. In mathematics, the English are indisputably pre-eminent in analytic number theory; the Russians are making important contributions in topology and probability, the French in algebra. America cannot match the group of European scientists in the important fields of enzyme chemistry and the organic chemistry of natural products. Nowhere else in the world can one duplicate or even approach the co-ordinated and co-operating Scandinavian group which is focusing so many precise techniques of chemistry and physics on problems of biology.

If one is tempted to question the vitality of science in Europe, it is interesting to note that the most dramatic scientific development of the year 1939 originated there, i.e., the splitting of the atom of the heavy element uranium and its transmutation into barium and other light elements. This realization of the old dream of the alchemists was based upon results obtained in 1934 by the Italian physicist Fermi; but the disintegration products of uranium were first directly observed in 1939 by Hahn and Strassmann of Berlin.

America needs to be humble about this question of intellectual leadership. In spite of the anxiety and insecurity abroad during these recent years, of the six Nobel prizes awarded in science in 1939, five went to Europe and one to the United States. In countless ways we are dependent upon Europe for stimulation and leadership in relation to many segments of our intellectual and cultural activity.

If because of war-exhaustion or chaos the universities and laboratories of Europe should be forced to suspend their fundamental activities for even half a decade, the consequences to the intellectual life of America would be immediate and disastrous. For scientific

growth is almost invariably the result of cross-fertilization between laboratories and groups in widely separated parts of the world. Only rarely does one man or one group of men recite with clear, loud tones a whole important chapter, or even a whole important paragraph, in the epic of science. Much more often the start comes from some isolated and perhaps timid voice, making an inspired suggestion, raising a stimulating question. This first whisper echoes about the world of science, the reverberation from each laboratory purifying and strengthening the message, until presently the voice of science is decisive and authoritative. Thus, in the case of the break-down of uranium during the past year, the early tentative questionings came from Rome; they were caught up at Berlin, were eagerly heard at Paris and Copenhagen, and then spanned the Atlantic and were seized upon here so enthusiastically that literally within hours, rather than within days, the critical experiments had been checked and extended at Columbia University, at the Carnegie Institution of Washington and in Lawrence's laboratory at the University of California.

Similarly, the amazing development and application of sulfanilamide—that beneficent gift to mankind—has been the result of a collaboration in which flags and boundary lines have been non-existent. The first hint of it was discovered in Germany, oddly enough in connection with the commercial dye industry, and the drug was given the name prontosil. With this hint as a basis, in 1935 a German scientist—Dr. Gerhard Domagk—published the results of his experiments with mice under carefully controlled laboratory conditions, showing the extraordinary effect of prontosil on streptococcus. The Pasteur Institute in Paris then picked the matter up, and subjecting prontosil to organic analysis discovered that its activity was localized in one distinctive part of its molecular structure. This potent factor in prontosil, separated from the rest of the molecule, is what we now know as sulfanilamide. At this point Queen Charlotte's Hospital in London, with a grant from the Rockefeller Foundation, tried the drug on women suffering from streptococcal infection associated with puerperal or childbirth fever, immediately reducing the death rate from such infections by 25 per cent. The Johns Hopkins School of Medicine was the next institution to carry forward the experiments, and in the last three years research on this drug has been developed, with brilliant results, in laboratories and hospitals on both sides of the Atlantic.

Achievement in science, more often than not, is the result of the sustained thinking of many minds in many countries driving toward a common goal. The curative spirit of man cannot successfully be localized or nationalized. Ideas are starved when they are fenced in behind frontiers. The fundamental unity of modern civilization is the unity of its intellectual life, and that life cannot without disaster be broken up into separate parts. If, as a result of the present cataclysm on the other side of the Atlantic, Europe freezes into an Arctic night, we shall not easily keep the fires lit in the universities and laboratories of America.

### ANNUAL REPORT OF THE MALARIA INSTITUTE OF INDIA FOR THE YEAR 1939

THE activities of the Malaria Institute of India are many and varied. Its functions are to advise the

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\*B.M.J., 1937, August 28. Page 412.

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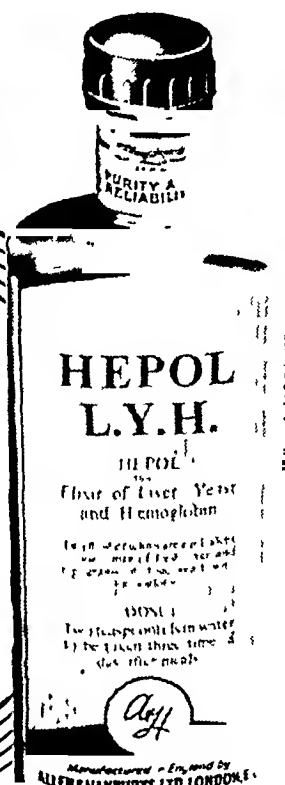
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Central Government and, where required, Provincial Governments and local bodies on all matters connected with malaria control, to carry out systematic research into the epidemiology and control of malaria and the bionomics of mosquitoes, to train medical officers in malariology, to act as a central bureau for the issue of publications dealing with malaria and mosquitoes and generally to advise and assist malaria workers throughout India. Close contact is maintained with malaria workers in other countries, both by correspondence and by the exchange of publications.

A six weeks' course in malariology for medical men is held annually at the field station, and many of the officers so trained are now doing valuable work in various parts of India. Nearly 300 students have undergone this training since the organization was first formed in 1927.

There are now thirteen publications produced by officers of the Institute in the Government of India Health Bulletin series. In addition to providing information for malaria workers throughout India, these publications are particularly valuable for teaching purposes, since they are kept continually up-to-date by the frequent issue of new editions.

An important function of the Institute is the testing of the various larvicides and insecticides which are used in malaria control work. Pyrethrum, which forms an essential ingredient of all insecticides, is now being grown successfully in this country, excellent results having been obtained with flowers grown in Kashmir, Kulu and the Nilgiri Hills. It is confidently expected that India will shortly be able to produce sufficient pyrethrum for her own needs and that an efficient insecticidal spray will eventually be made available at a comparatively low price. In this work, close contact has been maintained between the Malaria Institute and the Imperial Council of Agricultural Research.

The intensive anti-malaria campaign now in progress in Delhi urban area is being greatly facilitated by the recent transfer of the field station of the Institute from Karnal to Delhi.

The Delhi campaign is being carried out under the supervision and direction of the Malaria Institute. Three successive years of deficient rainfall render it impossible to assess with accuracy the value of the results achieved. Emphasis is laid on the fact that eradication of malaria from Delhi could only be achieved by converting the whole countryside into a barren desert but, states the report, it is confidently expected that as a result of this campaign the disease will no longer seriously affect the city's activities, as was formerly the case.

Officers of the Malaria Institute have been called upon to give advice regarding the rural anti-malaria schemes which have been initiated in various provinces as the result of a grant made by the Government of India. Field research units of the Institute have been working in the Wynaad, South India, and in the Terai district of the United Provinces in collaboration with two of the rural schemes. A third field research unit is carrying out investigations in Orissa in the vicinity of the Chilka Lake.

Laboratory researches include a number of important investigations on monkey malaria, of which several strains have been maintained. These have proved of great value for teaching purposes as well as affording abundant material for research work. Valuable results have also been achieved by the application of the precipitin test to mosquito blood meals. By this means it can be ascertained whether a particular species of mosquito feeds habitually on man or on cattle.

The report of the entomologist contains an account of a number of investigations regarding the life history and habits of various species of mosquitoes. Many collections of mosquitoes and other insects were received for identification during the year from all parts of India.

## ANNUAL REPORT OF THE PHYSIOLOGICAL SOCIETY OF INDIA, 1939

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# HEPOL L.Y.H

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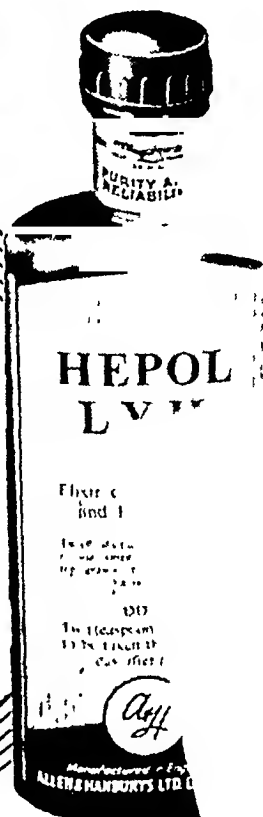
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Yeast is a rich source of the B vitamins. A yeast extract has been found effective in tropical macrocytic anæmia and in moderately severe cases of ordinary pernicious anæmia.

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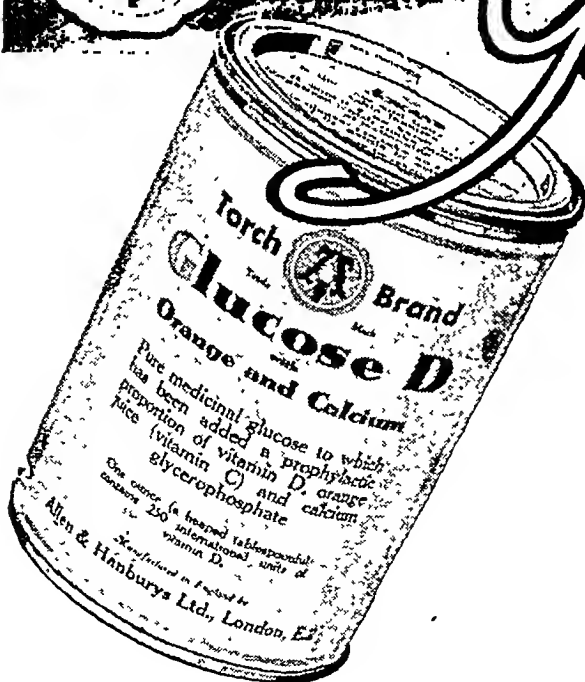


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Central Government and, where required, Provincial Governments and local bodies on all matters connected with malaria control, to carry out systematic research into the epidemiology and control of malaria and the bionomics of mosquitoes, to train medical officers in malariology, to act as a central bureau for the issue of publications dealing with malaria and mosquitoes and generally to advise and assist malaria workers throughout India. Close contact is maintained with malaria workers in other countries, both by correspondence and by the exchange of publications.

A six weeks' course in malariology for medical men is held annually at the field station, and many of the officers so trained are now doing valuable work in various parts of India. Nearly 300 students have undergone this training since the organization was first formed in 1927.

There are now thirteen publications produced by officers of the Institute in the Government of India Health Bulletin series. In addition to providing information for malaria workers throughout India, these publications are particularly valuable for teaching purposes, since they are kept continually up-to-date by the frequent issue of new editions.

An important function of the Institute is the testing of the various larvicides and insecticides which are used in malaria control work. Pyrethrum, which forms an essential ingredient of all insecticides, is now being grown successfully in this country, excellent results having been obtained with flowers grown in Kashmir, Kulu and the Nilgiri Hills. It is confidently expected that India will shortly be able to produce sufficient pyrethrum for her own needs and that an efficient insecticidal spray will eventually be made available at a comparatively low price. In this work, close contact has been maintained between the Malaria Institute and the Imperial Council of Agricultural Research.

The intensive anti-malaria campaign now in progress in Delhi urban area is being greatly facilitated by the recent transfer of the field station of the Institute from Karnal to Delhi.

The Delhi campaign is being carried out under the supervision and direction of the Malaria Institute. Three successive years of deficient rainfall render it impossible to assess with accuracy the value of the results achieved. Emphasis is laid on the fact that eradication of malaria from Delhi could only be achieved by converting the whole countryside into a barren desert but, states the report, it is confidently expected that as a result of this campaign the disease will no longer seriously affect the city's activities, as was formerly the case.

Officers of the Malaria Institute have been called upon to give advice regarding the rural anti-malaria schemes which have been initiated in various provinces as the result of a grant made by the Government of India. Field research units of the Institute have been working in the Wynaad, South India, and in the Terai district of the United Provinces in collaboration with two of the rural schemes. A third field research unit is carrying out investigations in Orissa in the vicinity of the Chilka Lake.

Laboratory researches include a number of important investigations on monkey malaria, of which several strains have been maintained. These have proved of great value for teaching purposes as well as affording abundant material for research work. Valuable results have also been achieved by the application of the precipitin test to mosquito blood meals. By this means it can be ascertained whether a particular species of mosquito feeds habitually on man or on cattle.

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justified. We are optimists and believe that there are men in this society with foresight, ability and leadership who can make this an accomplished fact. The lamp that has been kindled at Calcutta must throw its light throughout India. This may be considered an ambitious project but can be accomplished if the members of the society, amongst whom there are many leaders in Indian scientific circles, have the will to do it, and if active co-operation amongst them can be ensured.

In conclusion, we wish to thank all those who helped the society with their co-operation by communicating their papers and attending the meetings, and to the authorities of the various institutions where our meetings were held.

#### REPORT ON THE WORKING OF THE PUNJAB MENTAL HOSPITAL, LAHORE, FOR THE YEAR 1939

THE total number of patients under treatment at the Punjab Mental Hospital during the year under report was 1,299 against 1,235 in the preceding year. The daily average attendance was 1,038 and the maximum number on any single day was 1,058, of whom 843 were men and 215 were women. In order to remove the congestion in the female section and to provide for the growing needs of the hospital it was decided to build a double-storeyed block to provide additional accommodation for 100 female patients. The work was taken in hand during the year under report and has now been completed.

The number of patients who died in the hospital during the year under report was 47, compared with 32 in the previous year. The larger number of deaths was due to the fact that several patients newly admitted to the hospital were in an extremely bad state of health and could not survive for more than a few days. There were no cases of suicide, of death by violence or accident. The number of patients who were discharged from the hospital as cured was 112 against 84 in the previous year; while the practice of handing over harmless and chronic patients to their guardians was also resorted to more freely than before.

Excluding a sum of Rs. 45,363 spent on 'original works' the expenditure by Government on the maintenance of the hospital was Rs. 3,10,727 compared with Rs. 3,08,054 in the previous year. A sum of Rs. 2,04,294 was recovered from local bodies and the receipts from paying patients and other miscellaneous receipts amounted to Rs. 27,342. The net cost to Government was, therefore, Rs. 79,091.

Lieutenant-Colonel C. J. Lodge-Patch, M.C., I.M.S., who was the Medical Superintendent of the Hospital proceeded on leave on the 20th July, 1939, and Dr. R. S. Sharma, P.C.M.S., Deputy Medical Superintendent, was appointed to officiate for him.

#### ANNUAL REPORT OF THE NATIONAL ASSOCIATION FOR SUPPLYING MEDICAL AID BY WOMEN TO THE WOMEN OF INDIA (COUNTESS OF DUFFERIN'S FUND INCLUDING THE WOMEN'S MEDICAL SERVICE) FOR THE YEAR 1939

##### THE COUNTESS OF DUFFERIN'S FUND AND WOMEN'S MEDICAL SERVICE

THIS year owing to unavoidable re-investment of funds at lower rates of interest, the recurring income of the Countess of Dufferin's Fund amounted only to Rs. 33,000 approximately, instead of the usual Rs. 40,000. It was spent as usual on grants to Provincial Dufferin branches and hospitals as well as scholarships to medical students, 15 of which are available at the Lady Hardinge Medical College, Delhi, four in Bombay, three in Calcutta, and two in Madras. Of these, 14 are awarded from association funds and the rest from trust

funds under the council. The Gilchrist Trustees gave their annual grant of £150 for six of the Lady Hardinge Medical College scholarships, for which the council desire to record their cordial thanks.

The great events of the year have been the opening of the new Dufferin Hospital in Calcutta in March by Lady Reid, and that at Amraoti in August. They are both very satisfactory buildings, but it is much to be regretted that the Calcutta Hospital Committee has not had funds at its disposal to meet the urgent need for an up-to-date nurses' home, and the nurses have had to be allotted part of the hospital itself as quarters, so lessening the accommodation available for patients and the income from rent and fees. The accommodation for medical staff has also proved inadequate, as the new hospital needs an increased staff and private wards have had to be set aside for their use, again to the detriment of hospital receipts. It is much to be hoped that public interest will be aroused sufficiently for funds to be collected to remedy these defects at an early date.

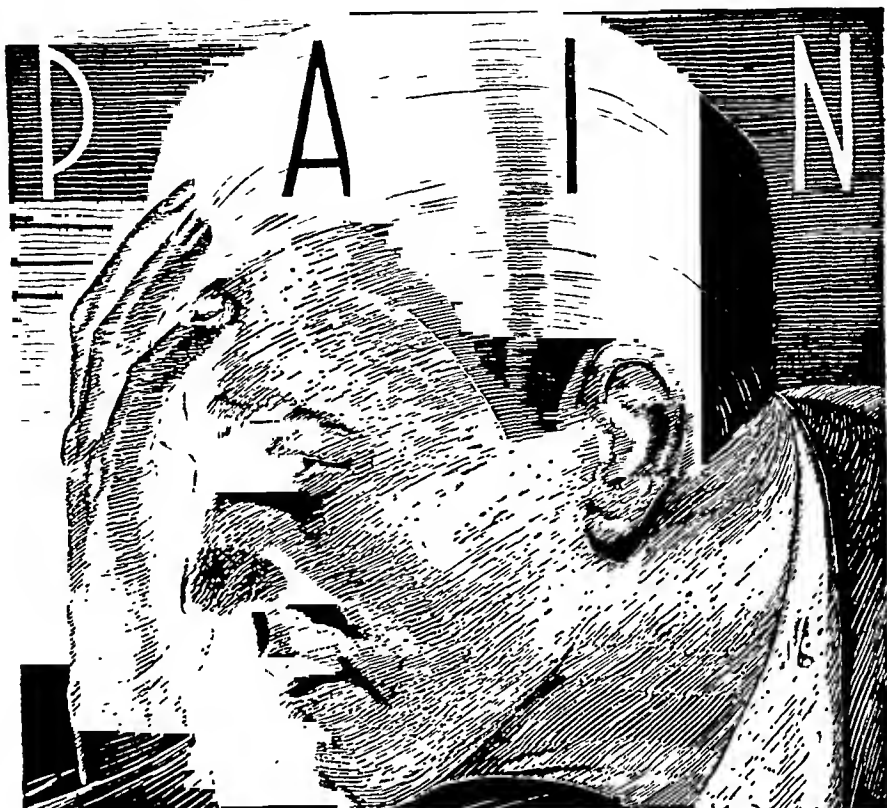
Amraoti on the other hand has provided very satisfactory accommodation for both its nursing and its medical staff, and is to be congratulated on its well-planned buildings.

Emphasis still needs to be laid on the great need for improvement in the nursing staff and the quarters provided for them in many of the hospitals. We can only repeat what has been said so many times before, that if the nursing profession is to take an honourable and leading place in the life of the country, then educated girls of good family must be willing to come forward in larger and larger numbers to train, and the local committees must see that the conditions of living are suitable for them, and they must not be expected to live in quarters grossly overcrowded or only fit for menials.

The financial condition of the Dufferin Hospitals as a whole is not satisfactory as so many are having a precarious existence owing to lack of endowments and local support, although their work is being more and more appreciated by the patients who come in increasing numbers and are willing to take any bed even on an open verandah rather than go on to whatever general hospital exists in the neighbourhood, this giving clear evidence that although the 'purdah' habit is breaking down in many districts, the demand for hospitals staffed only by women is stronger than ever and will remain even if 'purdah' should completely disappear.

It is to be regretted that the public still seem slow to realize the fact that medical relief, according to modern western methods, is expensive, and if they wish to obtain the services of highly qualified and experienced doctors such as the W. M. S. officers, and take the treatment required, they must be willing to contribute something towards the expenses in proportion to their resources. It is found that many middle and better class patients insist on occupying free beds in the general wards, though paying rooms are available, and at the most give a small donation to the poor box on leaving, even after confinements or operations, and so prevent the really poor from benefiting fully from the facilities offered. Most of the hospital committees are not willing to give the medical officer in charge authority to refuse admission to free beds to such patients and, in fact, often encourage the practice, with the result that the hospitals are in a chronic state of financial distress. Modern India, like other countries, needs to assimilate the fact that it can only afford free medical treatment to the really poor, and the general public must make a change in their attitude towards medical relief and be taught not to expect free advice and treatment unless they are really paupers. Only when this comes about will the hospitals be placed on a satisfactory basis.

The members of the Service maintained their reputation for efficiency during this year in spite of discouraging conditions, poor financial support and therefore limited staff, in many cases, and the fullness of their hospitals speaks well of their appreciation by those who so readily seek their aid.



## HEADACHE IS DISABLING

Headache may be as disabling as a grave illness. In migraine particularly, the headache is of all degrees of intensity, at times so severe as completely to incapacitate the sufferer. It is noteworthy how quickly the patient can obtain relief with Veganin. Composed of minimum doses of acetylsalicylic acid, phenacetin and codeine, Veganin affords striking proof of the superior analgesic potency of this synergistic alliance over that of its components administered separately. Recurrent painful conditions, such as migraine and dysmenorrhœa, yield with impressive promptness to the efficacy of Veganin.

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ber, 1939, of Captain J. G. Stonham, an officer the Indian Medical Service (Civil), lately in civil employment in Burma.

The Secretary of State for India has appointed Captain M. S. Zan to the Civil Branch of the Indian Medical Service, with effect from the 4th August, 1939, the date of his transfer to civil employment in Burma.

The services of Captain J. Guthrie, an officiating Surgeon, are replaced at the disposal of His Excellency the Commander-in-Chief, with effect from the 4th June, 1940.

On transfer to the Punjab, Captain H. H. Mahmood assumed charge of the office of Superintendent, Central Jail, Lahore, on the forenoon of the 10th July, 1940, relieving Lieutenant-Colonel G. A. Khan, Superintendent, Borstal Institute, and Medical Officer, Juvenile Jail and Female Jail, Lahore, of the additional charge.

#### PROMOTIONS

##### *Colonel to be Major-General*

A. C. Munro, K.H.P. Dated 12th March, 1940

##### *Captains to be Majors*

Dated 25th July, 1940

R. L. Raymond.

Dated 2nd August, 1940

R. J. Jarvic.

W. A. N. Marrow.

F. A. B. Sheppard.

M. Sendak.

Dated 3rd August, 1940

M. M. Mansfield.

#### RETIREMENTS

Captain S. P. Wauchoo. Dated 7th May, 1940.

Major G. J. Smith. Dated 3rd December, 1939.

## Notes

### CENTURIES OF USE

MEDICATION which has been in use for centuries—in fact since the earliest recorded periods of history—and still continues to have the most widespread use, must be looked upon, not so much as medication that has 'proved' itself, but as one of Nature's fundamental curative measures. Reference is made to the use of heat. Of the many forms of heat therapy available to the medical profession, physicians will find Antiphlogistine one of the most useful. It combines both prolonged moist heat and supporting medication.

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The booklet on Rutonal includes a selection of clinical reports on the use of this drug in a number of cases of epilepsy and copies may be obtained by members of the medical profession on request to Messrs. May and Baker (India), Limited, 11, Clive Street, Calcutta.

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## Original Articles

### A SCHEME OF CONTROL OF TUBERCULOSIS IN INDIA BY 'ORGANIZED' HOME TREATMENT

By C. FRIMODT-MÖLLER, C.B.E., M.B.,  
Ch.B. (Copenhagen),

*Medical Commissioner to the Tuberculosis Association  
of India*

EVERYONE who is acquainted with the conditions in India will probably admit that it is an extraordinarily difficult task to draw up a scheme for the control of tuberculosis in this vast country.

On the one side, there is a desire to introduce an ideal campaign, but against this have to be placed deplorably inadequate financial resources and other facilities for such a campaign, and nothing would handicap any campaign more than failure by an attempt to do the impossible. On the other side, there is often a surprising lack of understanding of how best to use such resources and facilities as are already available.

To have any real possibility of success, a scheme for combating tuberculosis in India must have duly balanced the object aimed at and the resources of money and personnel available, measures of prevention and measures of treatment, isolated anti-tuberculosis activities and a united front for tackling the whole tuberculosis problem.

The necessity for drawing up a balanced scheme is also brought home by a study of anti-tuberculosis activities in the West. There it will be seen that the tuberculosis policy has sometimes shown a swinging tendency and when it has swung out too far to one side by over-emphasis on certain aspects of the campaign then a set-back in that campaign has resulted. Naturally the campaign began with the attempt to treat all who suffered from tuberculosis in its manifest forms. When it was found that it was impossible to control the spread of the disease in this way, there came, in some responsible quarters, a period of disparaging institutional treatment as superfluous and too expensive, and all the emphasis was laid on raising the standard of living, improving hygienic conditions and educating the people about the nature of the disease by wholesale propaganda. But in spite of actual raising of the standard of living, of improving hygienic conditions and of wholesale propaganda in certain countries, the disease did not show the decline that was expected.

The result of this is that in some countries tuberculosis policy has swung back to treatment and isolation, but this policy goes now much further than it did before for two reasons: firstly, the discovery that there are many people suffering from tuberculosis with bacilli in the sputum who themselves do not know that they

are sick and therefore sources of infection to others, and, secondly, the technique of diagnosis has so improved that it is possible to find these preclinical sufferers from tuberculosis and to treat them. The finding of such 'carriers' is done through scientifically carried out tuberculosis surveys working from tuberculosis clinics equipped with all necessary facilities for this purpose.

Although the changes in the tuberculosis policy seemed at times to be even antagonistic, especially when there was overemphasis by their supporters, the general effect has, nevertheless, been not antagonistic but supplementary, and the present campaign in the West has drawn on all that was valuable in the various policies and has, in consequence, developed into a comprehensive, balanced and effective scheme. The war against tuberculosis utilizes every measure which can contribute its share to the defeat of the enemy. The tuberculosis policy is therefore now one of co-operation of state, local bodies, private bodies and the general public, with legislation, insurance measures and systems of more-or-less compulsory treatment and prevention.

#### *A balanced tuberculosis policy for India*

It is of no avail whatever to think that a balanced tuberculosis policy for India can be obtained by adopting that of the West. It is not only that the financial resources are so much smaller in India than in the West, but it is also that, even were considerable funds available, some of the other measures and facilities are lacking out of all proportion for a scheme on western lines to succeed in India.

What is the use, for example, of introducing compulsory notification of all tuberculous cases with compulsory modern treatment when the existing facilities for such treatment are completely negligible. In a country such as Scotland there is one bed for the treatment of tuberculous patients to each 900 of the population, which is almost enough for the treatment and isolation of all infectious cases. The lack of facilities for such treatment and isolation in India is fully borne out by the following figures. In Bombay presidency, where there is, proportionately to the population, the largest number of beds for tuberculous patients, there is one bed to about each 40,000 of the population; in the province of Assam with a population of more than 9,200,000 people there is not a single bed set aside for tuberculous patients, according to the *Indian Medical Review*, 1938.

Again, to take another example, even if sufficient beds and institutions could be made available, there is a great scarcity of doctors specially trained in modern methods of the treatment of tuberculosis and in dealing with the many aspects of the problems created by the disease.

In order to work out any tuberculosis policy for India it is therefore necessary to review not only the prevalence of the disease, but also the

existing anti-tuberculosis activities, and the resources available of both money and men. We have to keep in mind both the immediate campaign and the development of the campaign for the future, the creation of facilities for providing trained personnel, the place institutions are to have in the scheme, and the preventive measures which can and ought to be introduced with a reasonable prospect of adequate results.

In a country such as India where a raising of the general standard of living is likely to take generations and where, at the same time, the disease is on the increase, and the facilities for institutional treatment constitute the merest fraction of the enormous numbers of tuberculous patients, the emphasis in the control of tuberculosis must of necessity be on a campaign which concentrates all its efforts on striking at the real cause of the spread of the disease which is only one, namely, the source of infection.

The main object of the campaign must, therefore, be to search out the tuberculous patients in order to fight the disease where it exists and spreads. All efforts and resources must be directed to the anti-tuberculosis measures which will be particularly suitable for this object and which have already proved of value under Indian conditions. To these should be added only those other measures which can easily be adopted and developed and which can help to support the main campaign.

As it is beyond all possibility to construct even a small proportion of the tuberculosis hospitals and sanatoria necessary for institutional treatment of the two to five millions of tuberculous patients supposed to be suffering in India from active disease and needing treatment and care, there is no other way but to try to reach and help hundreds of thousands of the most dangerous sources of infection in their own homes by introducing organized home treatment and such other measures as would prevent them from spreading the disease to others.

#### *Organized tuberculosis home treatment*

Under the prevailing circumstances in India no tuberculosis policy which is balanced according to resources and measures available can be considered an ideal one. For a long time to come it will be useless to attempt such a scheme, but one must be content with the introduction of any scheme which from a practical point of view has a real prospect of success in reducing the death rate from tuberculosis and bringing substantial relief and cure to those who are suffering from this disease.

There is no reason to hide the fact that it has been clearly demonstrated in the West that institutional treatment and isolation of tuberculous patients bring far better results than any home treatment. But when institutional treatment on a large scale cannot be introduced, we need not stand idle or helpless when we can

concentrate our efforts on a scheme of control which will be immensely more effective than what is being done at present. If such a scheme could be successfully introduced it will be for the future to improve it when it becomes possible to do so, and to develop it along the lines which all would agree to be ideal.

It should be clearly understood from the very beginning that the scheme is not control by ordinary home treatment of the disease, but it is a scheme of control by 'organized' home treatment of tuberculosis which is quite a different thing. The word 'organized' implies the application of as much as possible of the modern specialized treatment and prevention to thousands of homes where at present patients are often left alone without any treatment whatever and without any preventive measures.

#### *Outline of the scheme*

There are five main measures or activities essential for a successful working of such organized home treatment, and the scheme as a whole, as well as its individual parts, will be considerably weakened even to the point of being useless, unless all the five measures are available and properly linked up as one chain of measures.

The five main activities are :—

- (a) The tuberculosis clinic.
- (b) Institutional treatment for a certain number of selected patients.
- (c) Close co-operation between the clinic and private practitioners.
- (d) Care and after-care committees to work in connection with the clinics and other tuberculosis institutions.
- (e) Colonies or settlements for tuberculous ex-patients.

#### *The place of institutions in the scheme*

It would be a great mistake to think that in the scheme of control of tuberculosis by organized home treatment there will be no place for tuberculosis institutions. Without such institutions the whole scheme would fail. They are the foundation for it and they form the basis from which the modern specialized treatment and prevention are to be carried into the homes.

On the other hand, the construction of a few more tuberculosis clinics, hospitals and sanatoria with a few thousand more beds is in fact, from a practical point of view, of no consequence whatever for an effective campaign, if the beds are to be used, as in the West, for the full course of treatment of pulmonary tuberculosis and for isolation of very infectious cases. But, if the institutions are established as a definite link in the chain of measures constituting organized home treatment, the increase of the number of beds now available even by only a few thousands is of the utmost importance to the whole campaign. The problem now to be tackled in

this connection is not the immediate construction of as many tuberculosis institutions as possible, but only as many as are absolutely necessary for the scheme in question without crippling the other measures equally essential for a successful working of a balanced scheme of organized home treatment and prevention. The necessity for the various kinds of tuberculosis institutions and their particular place in the scheme needs a brief explanation.

### *The tuberculosis clinic*

The tuberculosis clinic must have as its object prevention and, to a certain extent, treatment.

It is not necessary to go into detail about the various measures of prevention which the clinic should introduce in the homes of patients under the supervision of the doctors treating the patients, but two measures of prevention need to be mentioned.

One is the tuberculosis survey to be conducted by the clinic. Only by this is it possible to detect many persons carrying on their work and having tubercle bacilli in their sputum. The discovery of such carriers and the diagnosis of tuberculosis is a preventive measure of the greatest importance. In every large city in India there should be a tuberculosis clinic equipped with all modern facilities for diagnosis (a matter not always easy), which could be a consulting institution also for the doctors in the city.

The other measure of prevention needing mention is treatment which a clinic in India must give under the present circumstances. Artificial pneumothorax may be given as an example. By introducing this treatment, and in co-operation with the private practitioners controlling its effect, a great number of patients will be helped to get better in their homes, and approximately half of them will cease to have tubercle bacilli in their sputum and so cease to be sources of infection to others, while being treated in their own homes.

### *Hospital wards and sanatoria*

It is now possible by certain chest operations to cure many advanced patients in whom all other treatment has failed. These operations cannot be performed in a clinic but only in a fully-equipped tuberculosis hospital or sanatorium. The treatments referred to are, for instance, such operations as thoracoplasty, extra-pleural pneumothorax and other special operations, as well as treatment of spontaneous pneumothorax, certain forms of empyema, and other complications of various kinds. In the scheme of 'Control of Tuberculosis by Organized Home Treatment' these institutions therefore have their place.

In or near every large city there should be such a tuberculosis institution with 100 to 200 beds, but these beds should be reserved only for patients in need of the special treatment which cannot be given in their homes or in the

clinics, and after the special treatment the patients should return home for further treatment by the medical practitioners in consultation with the clinic doctor. In this way a small number of beds can become of the greatest value and play an indispensable part in the campaign.

These tuberculosis wards and sanatoria are also of great importance for the teaching and training of doctors. Without them the doctors in the city or province would have no opportunity of learning the modern methods of treatment and prevention for application in their practice. Teaching should, therefore, be given through post-graduate courses in these institutions and in the clinics.

### *Facilities for training of specialists*

For the training of tuberculosis specialists each province or larger state should have a well-equipped central sanatorium with at least 200 beds. Patients should be admitted to these institutions for their whole period of treatment and not just for the time of special treatment. Apart from the value to the patients themselves it is necessary that the doctors under training should follow the treatment from beginning to end. Only in such an institution will the doctors be able to get experience in all modern measures of treatment and prognosis of pulmonary tuberculosis.

It is, moreover, in such an institution that the best opportunity is found for research work on tuberculosis from the point of view of remedies against the disease, and such research work is indispensable in a place where specialists are trained.

Only doctors who have had long training and experience in such central institutions should be placed in charge of tuberculosis wards or sanatoria. These teaching sanatoria are best situated away from large cities in good climatic conditions.

### *Co-operation between clinic doctors and private practitioners*

No anti-tuberculosis campaign anywhere in the world has succeeded without close co-operation between the clinic and the private practitioners. The private practitioner must come to understand that the clinic is his best help and if this is to be so all competition between the two must be avoided. The clinic doctor should not be allowed private practice but should be compensated in this respect. Close co-operation with the clinic will increase the reputation of the private practitioner as the public will soon discover that his patients receive better and more specialized treatment.

Special arrangements will need to be made for poor patients who cannot afford to pay any fee to private practitioners. Unless these patients also are reached the campaign cannot succeed. The doctors who visit these patients, of whom there will be many, should have some

remuneration. This should be done through a care and after-care committee in connection with the clinic. This committee should pay a small fee to the doctor who visits and treats the poor patients, but only on the recommendation of the clinic doctor. He will assure the committee that the patient is really suffering from tuberculosis, that the patient is receiving the best treatment possible under the circumstances and that the proper preventive measures are being carried out in the home.

#### *Care and after-care committees*

Besides the work of a care and after-care committee in maintaining a close connection between the clinic and the private practitioner in caring for very poor patients already mentioned, it has other important functions. Among these are, helping the poor patient and his family either by food or by money, helping to isolate children from sick parents by placing them with relatives if possible or by caring for them in open-air shelters in day-time, and in finding suitable employment for patients restored sufficiently to work.

For expenditure connected with such work the care and after-care committee will need a fund. When it is seen that the most effective way of distribution of help to tuberculosis patients is through such a committee working in close co-operation with the clinic and other tuberculosis institutions, it will come to be realized that the committee should receive grants from Government and local bodies as well as subscriptions from the public. Support given to such a committee is not merely a charity but is also a self-defence against the disease.

#### *Colonies for tuberculous ex-patients*

There are always a number of patients who have very little hope of being able to maintain the good results of treatment when again exposed to the strain of their old conditions. They break down, and as tubercle bacilli usually reappear in their sputum, they become once more a source of danger to those among whom they live.

It is now more and more being recognized all over the world that in many patients the ultimate results of treatment depend to a great extent on the after-care, and that without this, much of the expenditure of skill, time and money in treatment is wasted. In the effort to help this class of patients various after-care schemes, such as colonies for ex-patients, have been brought into being. Experience has shown that a colony for ex-patients succeeds only when linked with a sanatorium and is justified only if it develops as a part of a combined institutional scheme.

The financing of an ex-patient's colony depends, of course, on the size of the scheme, but it is not impossible to introduce such colonies in India if adapted to existing conditions. There is already evidence to show that the beginning

of a colony in India can be made at a very low cost and that one may develop to be self-supporting, or nearly so, in maintenance expenditure. Such a colony should be constructed in simple village style with ordinary village houses only slightly altered to make them more open.

There are two great principles behind a colony, namely, medical help at hand for the colonists and work which give financial security for them.

A scheme of prevention would not become fully successful without such ex-patients' colonies. They should therefore be introduced gradually in connection with each large sanatorium.

#### *Propaganda*

In closing it is necessary to say a few words about propaganda in the campaign.

There are two kinds of propaganda which should be kept separate and which cannot be done at the same time.

The first and most important kind is the propaganda where the sick are found to be. It should concern only education of the patients and the persons in contact with them, with regard to the nature of the disease and the prevention of its spread among them. Such propaganda should, of course, stress the seriousness of the disease but it should not be overdone so as to frighten the people.

The second kind of propaganda is just as important for the whole campaign but is of a totally different type. This is the education of the general public through those sections of it which are able to understand it and benefit by it, such as colleges, schools and reading rooms and through activities such as the press and radio.

Such propaganda is very important in the beginning of the campaign. It will take a long time before it will be possible to see results of it, and there may be much disappointment and even many disappointing results. It is under these circumstances that a well-led propaganda campaign should set in and counterbalance any discouragement. It may be necessary to draw attention to that in the earlier stages of the campaign because the disease now hidden will come to light, it might seem that the disease is rather increasing than decreasing as the demand for treatment will be so much greater and more pressing than before. It should be explained that such a situation is really encouraging as it shows that the campaign is actually getting to grips with those problems which need solution first of all, and which need a general co-operation of all concerned to meet them satisfactorily.

#### *Co-operation*

The campaign in India will never succeed without something of that co-operation which in the West has brought so striking a decline of the death rate from tuberculosis. In the

(Continued at foot of opposite page)

## CHRONIC NON-TUBERCULOUS INFECTIONS OF THE LUNG

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### Introduction

CHRONIC non-tuberculous infections of the lung often simulate pulmonary tuberculosis in symptomatology, physical signs, clinical manifestations and even x-ray findings. Symptoms like cough, expectoration, dyspnoea, fever, pain in the chest, loss of weight, hæmoptysis, changes in the fingers and nails and signs arising from pathological changes, such as chronic catarrh, exudation, consolidation, excavation, fibrosis and the implication of pleural membranes, can be produced by non-tuberculous infections of the upper air passages, bronchial tubes and pulmonary parenchyma. There are cases in which pulmonary tuberculosis in an active or quiescent state and a non-tuberculous lesion due to other infections may be combined together.

The symptoms for which the patient approaches the doctor may be principally or entirely due to the non-tuberculous lesions. Wrong labelling in such cases may cause much inconvenience, mental worry and economic loss, by delaying or jeopardizing their recovery. To the general physician, as well as to the chest physician, a correct diagnosis, which can be obtained from a common-sense consideration of the history, physical examination, laboratory and x-ray investigation, is, therefore, of the greatest importance. To him, the first problem is to establish whether pulmonary tuberculosis exists or not; the next, in case pulmonary tuberculosis is present, whether it can explain the patient's symptoms and signs. In case he rules out pulmonary tuberculosis, he is confronted with the differential diagnosis of the pathological changes in the lung, and of the symptoms and other abnormal findings. The difficulties in diagnosis are increased when non-tuberculous lesions are unilateral and located in the upper lobe. In children giving a positive tuberculin test, the difficulties in diagnosis are further increased. Provided, however, a careful history

of the case is taken, clinical observations are carried out, x-ray and appropriate laboratory studies are made, a correct diagnosis can be established in most cases.

### Frequency

During the years 1938 and 1939, out of a total number of 14,052 new cases who attended the out-patients' section of the chest department of our hospital, only 3,111 or 22.1 per cent were labelled as pulmonary tuberculosis. 8.5 per cent of cases showed evidence of chronic bronchitis, 1.04 per cent of bronchial asthma, 0.5 per cent of bronchiectasis, and there was a small percentage that included pulmonary abscess, influenza, syphilis, pulmonary neoplasm, hydatid disease of the lung and pneumonocystosis. In 60 per cent of the cases, no lesions in the lungs could be demonstrated, which might interpret the symptoms. Some of these cases might have been due to foci of infection in the upper air passages or disease elsewhere than in the lung. It may be mentioned that all new cases attending the department are examined by fluoroscopy and that 88 per cent of the above cases were examined by radiography.

In a series of 1,877 non-tuberculous pulmonary disease cases admitted into the indoor medical wards of the Calcutta Medical College Hospital, where naturally serious cases are more commonly admitted, during the years 1937-39, the following incidence was noticed :—lobar pneumonia—647, bronchopneumonia—405, simple bronchitis—243, bronchial asthma—233, chronic bronchitis with emphysema—104, influenza—210, bronchiectasis—13, pulmonary abscess—18, pulmonary gangrene—1 and secondarily infected carcinoma of the lung—3.

In a series of 1,135 cases examined by me in my consultation chamber, where every case is examined under the x-ray screen and 95 per cent of the cases have been investigated by radiography, the following incidence was found :—pulmonary tuberculosis—50.5 per cent, chronic bronchitis, including bronchial asthma—11.8 per cent, bronchiectasis—3.4 per cent, pulmonary abscess—0.18 per cent, secondarily infected pulmonary neoplasm—0.15 per cent, cases in which no pulmonary lesions could be elicited—34 per cent.

In a series of 700 cases with chest manifestations and diagnosis reviewed by Dunham and Skavlem (1927), out of 574 cases admitted with a diagnosis of pulmonary tuberculosis, the diagnosis had to be changed in 166 (28.9 per cent) of the cases. Of these 166 cases, 72 were labelled as chronic bronchitis, 17 as bronchiectasis, 14 as heart disease and 6 as miscellaneous diseases outside the chest. Over 70 per cent of the cases of bronchitis and bronchiectasis were secondarily infected from infective foci in the upper air passages, indicating a close association between infection in the upper air passages and the lung.

*(Continued from previous page)*

West co-operation is a factor which now works automatically, co-operation between the tuberculosis institutions and the public as well as their doctors on the one hand, and on the other between the tuberculosis institutions and Government, local bodies, and voluntary tuberculosis associations.

In India such co-operation does not yet exist, but there is no reason not to work for it, and it is certain at least that it will never come into existence unless we work for it, determined to see it through. On this depends, ultimately, the success of all our efforts in fighting the disease on a nation-wide front.



In another series of 195 cases of pulmonary tuberculosis in America (Chapman, 1928), 57 per cent of whom consulted more than one physician, a wrong diagnosis was made in the following order (in patient's own words):—bronchitis—33, run down—19, influenza—17, non-tuberculous pleurisy—15, colds—8, pneumonia—5, nervous break-down—4, nervousness—4, spots on the lung—4, throat trouble—3, asthma—3, bad tonsils—3, tonsillitis—3, anaemia—3, catarrh—2, non-tuberculous laryngitis—2, intercostal neuralgia—2, ulcer of the stomach—2, overwork—2, weak lungs—2, no disease, cigarette cough, stomach cough, typhoid, intestinal 'flu', chronic (non-TB) ulcer of ear, chronic appendicitis, post-operative weakness, sinusitis, mastoiditis, thyroid trouble, elongated palate, weakness, rheumatism, whooping cough, (non-TB) rectal abscess, myocarditis, neurasthenia, hookworm, shell shock, spinal meningitis, catarrh of stomach and strained vocal cords—1 each.

#### SOME CHRONIC PULMONARY INFECTIONS WHICH MIGHT BE CONFUSED WITH PULMONARY TUBERCULOSIS

##### 1. *Unresolved lobar pneumonia and its sequelæ*

Acute caseous tuberculous pneumonia which is liable to be and sometimes is confused with lobar pneumonia, especially when the upper lobes are involved, need not be considered here, but some of the sequelæ of the latter, such as delayed resolution with prolonged convalescence, 'apical catarrh', abscess, bronchiectasis, chronic pulmonary fibrosis and empyema, may give rise to symptoms and signs which are likely to be confused with chronic pulmonary tuberculosis and pleural effusion of tuberculous origin.

True lobar pneumonia generally does not cause any actual destruction of tissue and leads to prompt resolution, but in caseous tuberculous pneumonia destruction of tissue is much more marked and cavity formation takes place. Not until the stage of destruction do tubercle bacilli appear in the sputum. In cases of delayed resolution of lobar pneumonia, the mottled x-ray appearance is not unlike that of tuberculous infiltration. But a carefully recorded history, clinical observation, x-ray investigation and blood and sputum tests help us to make an accurate diagnosis.

##### *An illustrative case*

H. S., Punjabi Hindu male, 43 years, transport worker.

*Clinical history.*—In February 1939, had pneumonia of right lung, followed by recovery. In May 1940, had again pneumonia of the right lung. Patient first attended the chest department on 11th June, 1940, with a history of cough, expectoration, fever 99°F. to 102°F., pain in right chest and dyspnoea on exertion for a month since the attack. Sputum was negative for tubercle bacilli thrice, even by concentration method. Sedimentation rate of red cells—88 mm. at end of first hour.

*Physical examination.*—Increased vocal fremitus, impaired resonance and râles over the upper and middle zones of the right lung. The appearances of the chest skiagram taken on 11th June, 1940, are shown in

figure 1, which shows extensive mottling, more marked in the lower zones, not unlike tuberculous infiltration but more homogeneous. This appearance and the negative sputum led us to label the case as delayed resolution in pneumonia and accordingly a course of M. & B. 693 was given. The patient became free from symptoms and signs within two weeks. The appearances of a skiagram taken on 5th July shows (figure 2) the clearing up of the mottled area. The diaphragm is also slightly raised owing to fibrosis.

The naso-pharyngeal investigation showed a deviated septum with spur, hypertrophy of the turbinates, septic tonsils and chronic pharyngitis.

##### 2. *Some sequelæ of broncho- or lobular pneumonia*

Although the acute condition is generally due to a mixed infection with pneumococcus, streptococcus, staphylococcus, bacillus influenzae, bacillus of Friedlander and *Micrococcus catarrhalis*, the cases due to streptococcus and influenza bacillus are more liable to become chronic, thus simulating changes more commonly met with in the bronchopneumonia of tuberculous origin.

In the more acute cases, one might have to differentiate between typhoid and paratyphoid fevers. In milder cases, where the duration extends beyond three or four weeks, one is required to differentiate between tuberculous and non-tuberculous cases. The age, location and distribution of the lesions, repeated sputum examination (stomach-wash sediment in infants and children), blood and x-ray examination, besides clinical observation, should be taken into consideration in arriving at the diagnosis.

##### 3. *Chronic bronchitis of infective origin*

Recurrent attacks of acute bronchitis, often due to secondary infection from the upper air passages (tonsils, adenoids, nasal sinuses), damage the bronchial mucosa and walls and make them more vulnerable to further attacks until the condition becomes chronic. Climate and season seem to have some influence in precipitating or perpetuating attacks, winter and the rainy season being considered unfavourable. The relationship of atmospheric conditions to the production of these physical abnormalities is not well understood but recent work done in France indicates that alterations in ionization of the atmosphere may create an imbalance in the neuro-vegetative system and may aggravate the effects of infection already present.

In a large majority of cases of chronic bronchitis (93 per cent in our series), septic conditions have been found in the naso-pharynx, and/or nasal sinuses. In Dunham and Skavlem's series (*loc. cit.*) 72 per cent showed infection in the upper respiratory tract. In most of these cases of chronic nasal infection, there is postnasal discharge. From the way tracheally introduced lipiodol travels down the bronchi into the bronchioles and pulmonary tissues, there is no doubt that in these cases septic material trickles down the tracheo-bronchial passages and keeps up the bronchial catarrh. The routine examination of the nose and throat



and x-ray examination of the nasal sinuses are, therefore, important in investigating a case of chronic bronchitis.

The infective material in the bronchial tubes produces a chronic cough with a variable amount of expectoration, occasional fever during acute exacerbations or a long-continued low type of afternoon fever, occasional streaks of blood, a substandard state of health and some degree of dyspnoea in cases of bronchospasm and emphysema. The damaged bronchial walls may lead to dilatation of the tubes and peribronchial changes, producing various types of bronchiectasis. Usually most cases follow an incompletely recovered acute bronchitis but there are many in whom the course has been chronic from the commencement. In children with enlarged tonsils and adenoids, along with cough, an under-developed condition is presented. These symptoms should be enough to induce the patients to suspect pulmonary tuberculosis and promptly to seek medical aid but actually the delay is much longer than is anticipated. In a series of 1,200 cases that attended the chest department of our hospital and in 134 of my private cases, the following figures have been obtained:—

Duration	Hospital series	Personal series
Below 1 year ..	877	76
Between 1-3 years ..	134	31
" 3-5 " ..	73	12
" 5-10 " ..	78	8
Above 10 " ..	38	7

#### Age and sex distribution

**Age.**—Out of 1,200 hospital cases, 72 were below 10 years, 200 between 10 to 20 years, 441 between 20 to 30 years, 275 between 30 to 40 years, and 212 above 40 years. Among 134 cases in my personal series, 13 cases were below 10 years, 20 between 10 to 20 years, 49 between 20 to 30 years, 26 between 30 to 40 years and 16 above 40 years.

**Sex.**—More males attended the department with chronic bronchitis than females. Thus, in the hospital series, 957 males and 243 females were diagnosed, while in my personal series, 99 males and 35 females were diagnosed as chronic bronchitis.

Five to ten per cent of the bronchitis cases came with complaints of bronchospasm or bronchial asthma. It has already been pointed out that quite a large percentage of these cases showed the existence of septic conditions in the upper respiratory tract. How far the infective element was responsible in the production of the condition it is difficult to say, but in a fair number of cases the attacks begin with 'colds' or influenza-like onset, with or without some fever. The question of genesis and pathology of these cases in this country is far from settled,

but a few laboratory investigations carried out may be of interest.

Nine out of the 1,200 cases in the hospital series showed evidence of some degree of bronchiectasis by lipiodol bronchography. Only one case showed tubercle bacilli in the sputum without any evidence of parenchymal infiltration. Two cases had a syphilitic origin, both being relieved by anti-syphilitic treatment. In investigating the cases of chronic bronchitis, radiography was utilized in 30 per cent of the hospital cases and 97 per cent of my private cases.

**Sputum.**—The sputum is usually muco-purulent and in cases of putrid bronchitis it may have an offensive odour. The sputum may be intimately mixed or streaked with blood. The bacterial flora present shows mainly streptococcus, *Micrococcus catarrhalis*, some diphtheroid bacilli, staphylococcus, Friedlander's bacillus, bacillus influenzae and pneumococcus. In ulcerative and putrid bronchitis, a specific group of anaerobic micro-organisms, of which spirochaetae (*T. microdentium*, *T. macrodentium*, *S. vincenti*, *S. bronchialis*), fusiform bacilli, vibrios and cocci are the most important, are often present.

**Blood changes.**—A variable degree of eosinophilia is present in a large percentage of cases. Out of 366 cases in which a diagnosis of chronic bronchitis was made at the out-patients' section of the chest department, the percentage of eosinophile cells and the incidence of eosinophilia is shown in the following table:—

TABLE

Percentage of eosinophiles	PERCENTAGE INCIDENCE	
	Hospital cases	Private cases
Under 5 ..	55	11
5 and under 15 ..	24	40
15 " " 25 ..	6	9
25 " " 40 ..	6	11
Over 40 " ..	9	29

Eosinophilia was more pronounced in cases with less than three years' duration than in more chronic cases and particularly marked in cases with a duration of less than one year. Acton and Dharmendra (1933) noticed a high blood eosinophilia in bronchitis cases infected with a group of Gram-negative bacilli allied to Friedlander's bacillus or *Eberthella phaffi*. They (Acton and Dharmendra, 1933a) also noticed a shift to the left in Arneth count and a high Arneth index in cases of infective bronchitis. Napier and Dharmendra (1936) observed that, in these cases, auto-vaccine therapy brought about a reduction of the shift to the left in Arneth count.

It may be pointed out, in this connection, that there is a large group of cases in which the blood eosinophilia is not marked but in which

## PULMONARY TUBERCULOSIS AND DIABETES MELLITUS

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It is generally recognized that the incidence of tuberculosis in diabetics is higher than in the general population. Root and Bloor (1939) found that in a series of 1,659 diabetic patients in a Boston (U. S. A.) hospital, 2.5 per cent showed also active pulmonary tuberculosis, which was probably about five times as great as would be expected in the non-diabetic population.

It is also recognized that when pulmonary tuberculosis develops in a diabetic, it is of a serious type, and some workers have estimated that when diabetics develop pulmonary tuberculosis, 70 per cent die of the tuberculosis.

In this paper we shall review a series of 157 patients with both diabetes and pulmonary tuberculosis, who were found among 7,205 patients treated in the Union Mission Tuberculosis Sanatorium, Arogyavaram, between 1918 and May 1940.

### *Sex and age incidence*

Of the 157 cases, 133 were men, and 24 women, but no deductions can be drawn from the wide difference in these figures, although the difference is considerably greater than that in the number of men and women patients in the institution.

The age incidence among the 157 patients with both diabetes and tuberculosis is shown in table I.

(Continued from previous page)

Dr. I. Ellias, medical registrar, Medical College Hospital, Calcutta, for kindly compiling the figures of cases in the medical wards for me.

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It will be seen from the table that only 34 or 21.7 per cent of the diabetic patients were below 35 years of age and that comparatively few cases of diabetes were found among the tuberculous patients in the same age group—namely, only 34 out of 5,707 (0.59 per cent). Above the age of 35, there are 123 diabetics out of 1,175 tuberculous patients (10.46 per cent). According to our experience, therefore, diabetes is frequently associated with tuberculosis after the age of 35, and should always be looked for in the older tuberculous patients.

TABLE I

*Classification of diabetics and non-diabetics according to age group*

Age group in years	Total number of diabetics and non-diabetics	Number and percentage of diabetics
0-5 ..	9	..
6-10 ..	73	..
11-15 ..	314	..
16-20 ..	1,307	2
21-25 ..	1,751	2
26-30 ..	1,386	10
31-35 ..	567	20
36-40 ..	561	36
41-45 ..	323	27
46-50 ..	172	35
51-55 ..	70	15
56 and up	49	10

### *Relationship between the onset of pulmonary tuberculosis and diabetes*

It has been found in our series of 157 cases that 115 (73.2 per cent) gave a definite history of diabetes prior to the onset of pulmonary tuberculosis. In 38 (24.2 per cent) cases their diabetic condition was not known, and no investigation for diabetes was done prior to admission into the sanatorium for the treatment of pulmonary tuberculosis. In two cases diabetes was recognized only six months after the onset of pulmonary tuberculosis, and in two cases diabetes and pulmonary tuberculosis were diagnosed simultaneously. These findings support the view held by many that, where both diseases co-exist, in the majority of cases diabetes antedates the onset of pulmonary tuberculosis. In the 115 cases where diabetes was recognized before the onset of pulmonary tuberculosis, the period of diabetic life before tuberculous affection was recognized was as follows:—

TABLE II

*The period of onset of diabetes before that of tuberculosis*

Length of period	Number	Percentage
Four years and below ..	73	63.5
Above four years ..	42	36.5

PLATE XIV  
CHRONIC NON-TUBERCULOUS INFECTIONS OF THE LUNG

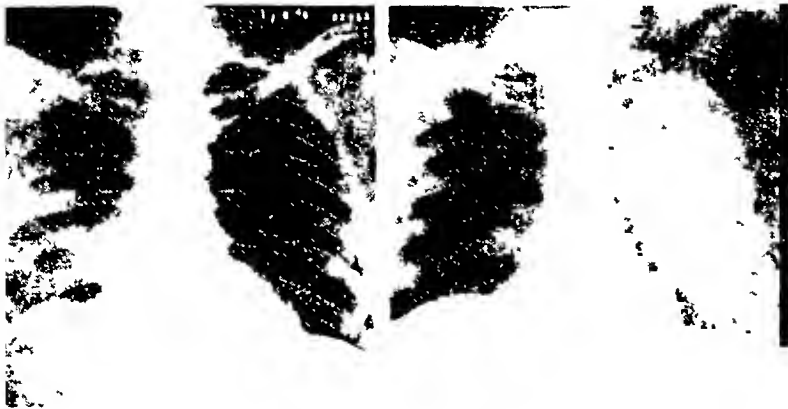


Fig 1

Fig 2.



Fig 3

Fig 4



Fig. 8.

Fig. 9.

*Descriptions—*

Figs 1 and 2—Delayed resolution in pneumonia.  
Fig 3 and 4—Chronic pulmonary abscess.  
Figs 5, 6 and 7—Bronchial carcinoma.  
Figs 8 and 9.—Pulmonary sarcoma.



Figs. 5, 6 and 7.

PLATE XV  
PULMONARY TUBERCULOSIS AND DIABETES MELLITUS

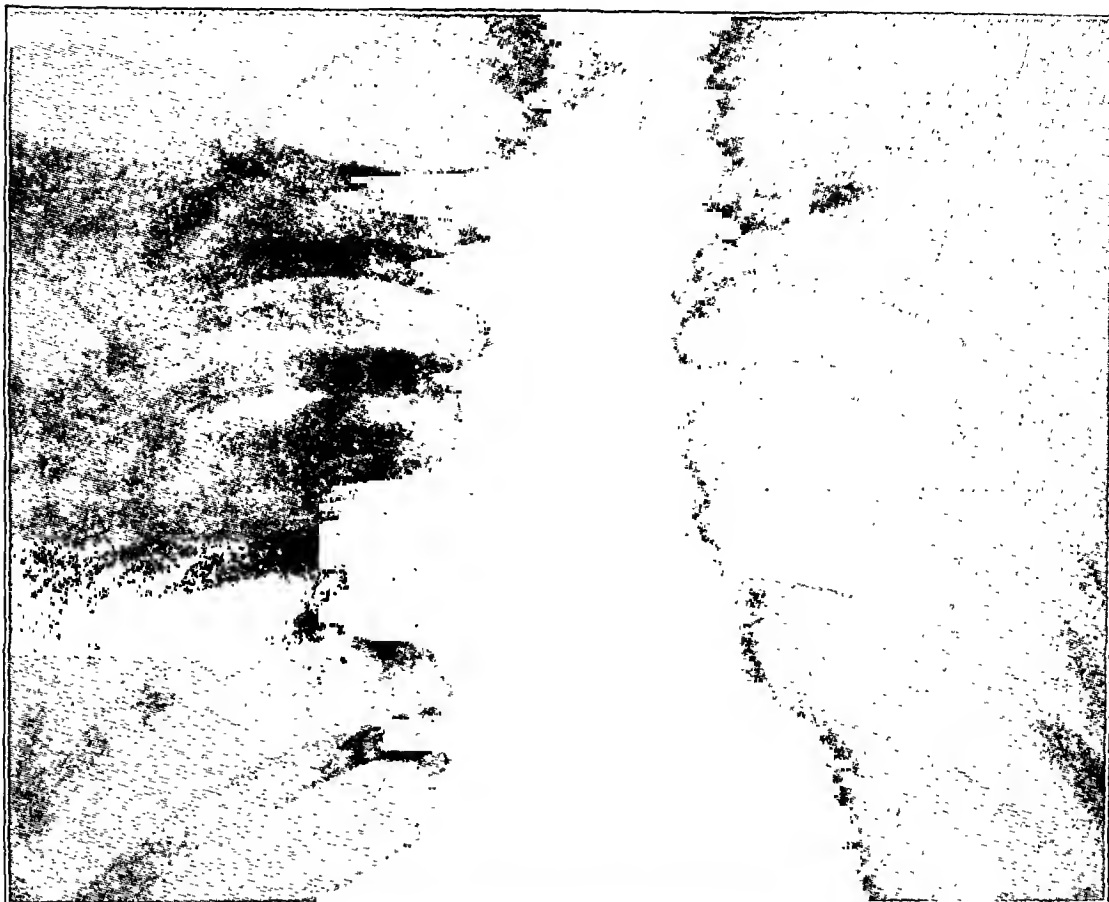


Fig. 1.

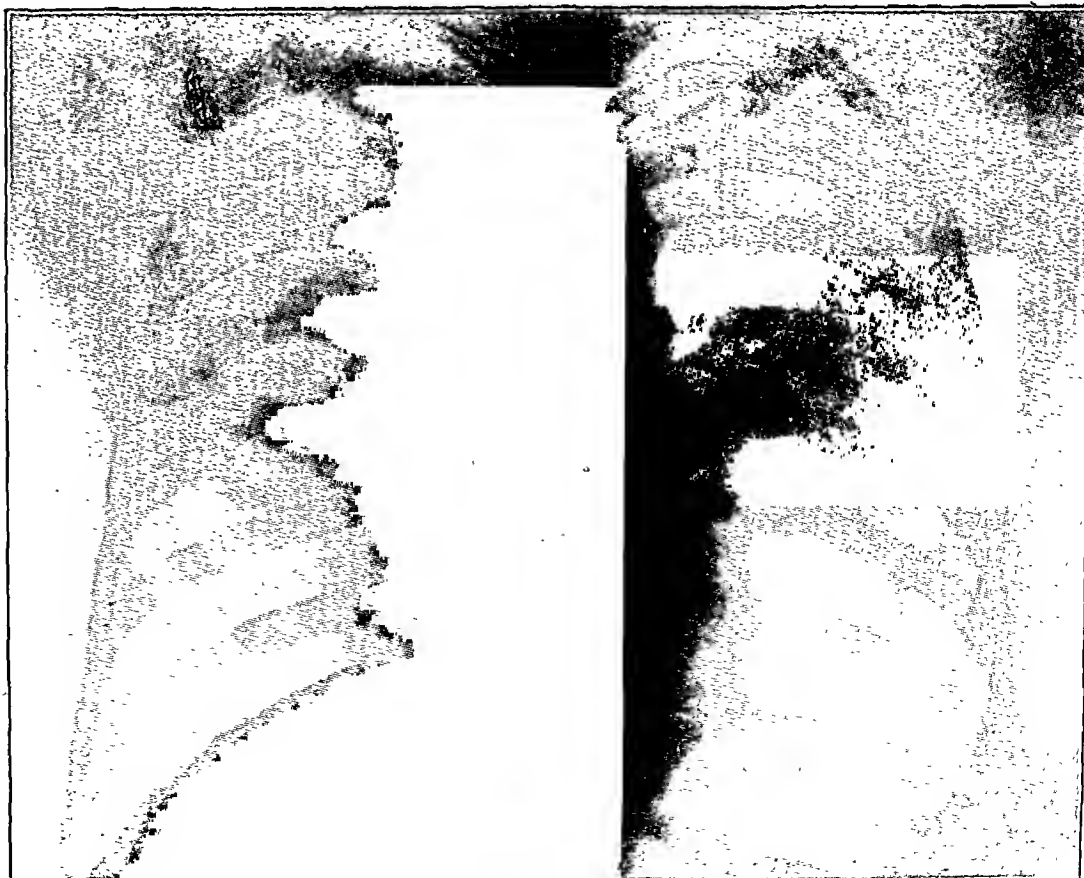


Fig. 2.

From table II it will be seen that in these patients the tuberculosis developed before four years in 73 (63.5 per cent).

#### *Type of tuberculosis as studied by x-ray*

It has been possible to study the x-ray films in 112 of the 157 cases, films not being available for some of the earlier cases. With a view to determining the type and severity of the tuberculous disease, the following points were observed, namely, the amount of fibrosis, tendency to dissemination, whether one or both lungs were involved, and the amount of cavitation. This is shown in table III.

TABLE III  
*Type of disease as judged by x-ray study in 112 cases*

Type	Number	Percentage
Exudative .. ..	83	74.1
Fibrotic .. ..	3	2.6
Mixed .. ..	20	17.8
Caseo-pneumonic .. ..	6	5.3
Unilateral .. ..	44	39.2
Bilateral .. ..	68	60.7
Localized .. ..	26	23.2
Disseminated .. ..	86	76.8
Cavities { Single .. ..	42	37.5
{ Multiple .. ..	58	48.2
Thick perihilar involvement ..	35	31.3

The findings in the above series are not materially different from those found by Benjamin (1938) for a series of 2,021 Indian patients suffering from tuberculosis. On the other hand, although in general there is not any appreciable difference in type, the character of the exudative reaction in diabetics tends to be more severe, and the lung shows a thick shadow similar to that in lobar pneumonia. This usually covers the entire middle zone, including the perihilar region. The two illustrations (plate XV) show a typical tuberculous process in diabetic patients.

#### *Treatment*

In the earlier years, the combination of diabetes and tuberculosis was considered to present an almost hopeless prognosis. The advent of insulin and artificial pneumothorax and other measures of collapse therapy have completely altered the outlook.

To get good results both the tuberculosis and the diabetes have to be treated simultaneously. If the diabetes cannot be controlled by diet alone, insulin has to be given. The diet, however, has to be more generous than in diabetes uncomplicated with tuberculosis.

If the lung indicates some form of collapse therapy, this should be instituted irrespective of the presence of diabetes, provided the diabetes is treated at the same time. If the diabetes is carefully regulated, surgery is no more dangerous than in the average non-diabetic case.

In 145 patients treated for more than one month, unilateral pneumothorax was done in 69, simultaneous bilateral pneumothorax in 6, phrenico-exsaisis in 9, thoracoscopy and cauterization in 11, and rib resection for empyema in 1. No thoracoplastics have been done in this series, but this is not because the patients were diabetic, but because the types of lesion in the lungs were not suitable for this operation.

Diabetes is not a contra-indication to gold therapy. In our series sanoerysin has been given in 21 cases.

#### *Complications during treatment*

The following complications were found during treatment of the 145 cases with tuberculosis and diabetes :—

Laryngeal tuberculosis .. ..	8
Intestinal tuberculosis .. ..	1
Glandular tuberculosis .. ..	1
Spontaneous pneumothorax .. ..	4
Pleurisy with effusion .. ..	5
Dry pleurisy .. ..	3
Effusion in artificial pneumothorax ..	50
Empyema .. ..	7
Hæmoptysis .. ..	60
Fistula-in-ano .. ..	10

In addition, there was the diabetic complication of ketosis as a terminal symptom in two patients.

The above tuberculous complications are what are usually found in non-diabetic tuberculous patients: the only points of significance are that effusion in artificial pneumothorax is slightly higher, 66.7 per cent as against 54.2 per cent in the non-diabetic patients, and bleeding from the lungs occurred in 60 (41.4 per cent) as against 34.3 per cent for the whole number of patients. Of the patients with hæmoptysis, in eight the hæmorrhage was the immediate cause of death.

#### *Stage of disease and immediate results of treatment*

Of the 157 patients, 12 are excluded in the analysis of results of treatment, as their period of observation was less than one month.

Of the remaining 145 patients, one was in stage I, 14 in stage II, and 130 (or 89.7 per cent) were in stage III. In the classification of the stage of disease, it is accepted as a general principle that pulmonary tuberculosis complicated with diabetes is classified one stage worse than it would have been without diabetes unless there are other serious complications. In the present series of patients, however, this has not had much effect, as the majority were already in stage III, apart from the question of diabetes.

The results of treatment are shown in table IV :—

between one year and two years, and 1 after between two years and three years.

TABLE IV

*Classification of 145 cases according to the stage and immediate results of treatment*

Stage	Number	Arrested	Much improved	Improved	Percentage of positive results	Stationary	Worse	Died
I	1	..	1	..	..	..	..	..
II	14	1	7	2	..	1	3	..
III	130	..	28	32	46.1	23	22	25
TOTAL	145	1	36	34	..	24	25	25

Of the 130 cases in stage III, positive results were obtained in 60, or 46.1 per cent, as against 55.5 per cent of positive results in 3,130 stage III cases without diabetes.

Of the 145 patients, 25 (17.2 per cent) died during treatment; the immediate cause of death was in 16 progressive tuberculosis, in 8 severe hæmoptysis, and in 2 diabetic coma.

If the results are classified according to the severity of the diabetes, we find that we can analyse the results in 112 patients; in 33 patients who belonged to the earlier part of the period reviewed, the blood sugar estimation was not done. The results are shown in table V.

It will be seen from table V that positive results were obtained in 3 (30 per cent) of the cases of mild diabetes, in 24 (44.4 per

If we group together the patients who died in the sanatorium and those known to have died after discharge, we find that 63 out of 76 patients, whose fate is known, have died within three years. This means that so far the ultimate results of treatment are not good. The explanation of the discrepancy between the immediate results and after results is that probably the patients were unable to maintain the improvement, because they could not continue the strict treatment necessary for both diabetes and the tuberculosis, as in only one case was the tuberculous disease completely arrested.

#### Summary

(1) A review is made of 157 patients suffering from both diabetes and tuberculosis.

TABLE V

*Classification according to severity of diabetes and immediate results of treatment*

Severity of diabetes	Number	Arrested + much improved + improved	Percentage of positive results	Stationary and worse	Died
Mild (blood sugar below 200 mg. per cent)	10	3	30.0	5	2
Moderate (between 200 and 300 mg. per cent).	54	24	44.4	18	12
Severe (above 300 mg. per cent) ..	48	21	43.7	16	11
GRAND TOTAL ..	112	48	..	39	25

cent) of moderate diabetes, and in 21 (43.7 per cent) of severe diabetes. The severity of diabetes does not seem to affect the results of the treatment when the diabetes is controlled.

#### After results of discharged patients

In assessing the value of treatment it is necessary to follow up the cases after discharge.

Of the 120 patients who were discharged from the sanatorium, it has been possible to trace 51. An analysis of the 51 cases shows that 38 (74.5 per cent) have died. Of the 38 dead, 28 (73.7 per cent) died within six months of discharge. 5 between six months and one year, 4

(2) Figures are given of sex and age incidence.

(3) The relationship of onset of diabetes and tuberculosis is discussed.

(4) The type of tuberculosis in diabetics is not materially different from that in non-diabetics in India, except that the exudative reaction seems more severe.

(5) Diabetes is not a contra-indication to any of the usual forms of treatment of tuberculosis, including surgery.

(6) Hæmoptysis was seen more frequently in the diabetic group than in the non-diabetic.

(Continued at foot of opposite page)



## SPONTANEOUS PNEUMOTHORAX

By W. G. JONES, B.Sc., M.D.

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SPONTANEOUS pneumothorax is a subject about which we all know something but do not know enough. In this article, no attempt is made to cover the subject exhaustively, but with the purpose of gathering together current views and interesting information that should profit those of us who are learning how to treat conditions in that heretofore rather unknown continent, the chest.

There are three kinds of pneumothorax: induced (artificial) or therapeutic; spontaneous or that produced without external influence; and traumatic, caused by external influences. It is better to apply the term spontaneous pneumothorax to all cases whether primary or secondary to some known pathological change, and to reserve the term idiopathic spontaneous pneumothorax for those cases when there is no evident cause for this condition. A superimposed spontaneous pneumothorax is the term used when it occurs in the course of an artificial pneumothorax.

It used to be thought that spontaneous pneumothorax was due to tuberculosis only but this is far from correct. Post-mortem studies reveal a large number of causes, although tuberculosis is certainly the most common one. Of 918 autopsied cases (Goldberg, 1935)

		Per cent
Tuberculosis was found in ..	715	77.8
Gangrene and empyema ..	110	12.0
Wounds ..	32	3.5
Bronchiectasis, abscess, emphysema, infarct and paracentesis	34	3.7
Caries or abscess of chest wall, perforation of viscus or gland, etc. ....	11	
Cause undetermined ..	16	3.0
	918	

Thus we see that spontaneous pneumothorax is caused by all types of pulmonary diseases, especially those associated with a focus of necrosis situated close to the visceral pleura. In children it may occur more commonly in

(Continued from previous page)

(7) The immediate results of treatment of tuberculosis in diabetics is good, but slightly below the average for non-diabetics.

(8) The after results have been discouraging so far and point to the necessity of very careful control of both diabetes and tuberculosis, if the improvement gained during treatment is to be maintained after discharge.

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association with a streptococcal or staphylococcal bronchopneumonia, or in those diseases producing a violent cough, such as pertussis or asthma.

But spontaneous pneumothorax is by no means found only at the post-mortem table. Laennec in 1819 recognized an 'idiopathic' variety without obvious pathology which was found in apparently healthy people. Until 1932, however, the literature contained only scattered reports of such cases, and the first series (51 cases) was reported in that year by Kjaergaard (1932) of Copenhagen. Since then many such series have been published. This increase in idiopathic cases reported in the past 10 years is due to the more widespread diagnostic use of the x-ray in all types of chest condition. Negative tuberculin reactions were reported in about half of all cases classed as spontaneous pneumothorax without other 'evident pulmonary pathology. Without the use of x-rays the failure of diagnosis is due to the transient nature of the subjective complaints in the majority of instances, and the rapid complete recovery on simple rest treatment.

The cause of simple idiopathic spontaneous pneumothorax in an apparently healthy person is not very clear. Laennec (Kirshner, 1939) thought it arose from the rupture during coughing, sneezing, straining, or other spasmodic effort of an emphysematous bleb on the surface of the pleura. Some claim to have actually seen such blebs at autopsy, but 'idiopathic' cases seldom come to the autopsy table. It is thought that these blebs represent air which has come from the rupture of an alveolus or terminal bronchiole and which has then 'dissected' along the interstitial tissue to the pleura. In rare cases the air proceeds centrally and is then found subcutaneous, having reached the skin of the neck *via* the mediastinum. Others incline to attribute the rupture to a weak 'congenital defect' or to a weak spot at a scar.

At all events the majority of these cases present transient symptoms, and there is as a rule no pleural reaction or exudate. Many cases of recurrent spontaneous pneumothorax on one or both sides are reported in the literature. The symptoms depend on the extent of the pneumothorax and the suddenness of its onset. This depends on the size of the pleural tear and its type—closed, open or valvular. In the simple cases the tear soon closes and the air is absorbed without complications. The open types, producing a persistent pneumothorax fortunately are rare, in this group. A small tear may become closed with the onset of exudate (spontaneous or induced) or by further collapse of the lung.

The valvular type produces a 'tension pneumothorax' which can give alarming symptoms very suddenly. The mechanism of these valves has been studied by Zavod (1939) who describes three types:—(1) the flap valve, produced by an incomplete tear at the pulmonary insertion

of an adhesion; (2) the slit valve, as made by a stab wound of the lung, or a longitudinal laceration of the lung by the point of a needle; and (3) the purse-string valve, an ulcerative opening from a peripheral cavity.

We have ourselves seen recently a patient of thoracoplasty with a contralateral pneumothorax who developed alarming symptoms of spontaneous pneumothorax on three successive occasions when an increased amount of air was given on the pneumothorax side. He must have had a valve type of laceration that opened up with greater lung collapse.

The chief symptoms of spontaneous pneumothorax are pain in the chest, dyspnoea and shock; or there may be few or no symptoms at all. Much depends on the suddenness of onset and extent of collapse. This diagnosis should be kept in mind in all kinds of pulmonary disease, and in pulmonary tuberculosis at all times. Joress (1936) has called attention to the fact that severe abdominal pain, often with persistent nausea and vomiting, is a not uncommon symptom of spontaneous pneumothorax, and may be very misleading. In some cases the onset is sudden, at other times it is gradual. The abdominal pain may be accompanied with local signs (muscular rigidity, etc.) and when dyspnoea and other chest signs are absent the diagnosis is easy to miss. The production of pleural fluid (as the evidence of the pleuritis which is the basis of the referred pain to the abdomen) may be delayed for days or weeks and hence this diagnosis should not be dismissed too quickly.

Spontaneous pneumothorax is of course most common and often a serious complication in pulmonary tuberculosis. Its incidence is given by Young (1936) as 10 to 14 per cent. It is especially common in bilateral pneumothorax. Mattill and Jennings (1940) report it in 21 per cent of 144 bilateral pneumothorax cases, in which the limited respiratory reserve makes a spontaneous pneumothorax readily detected. In the presence of advanced pulmonary tuberculosis death may occur early from shock, exhaustion or heart failure. The rupture of a pleural tubercle is a frequent cause in many cases.

For the practising physician who is treating tuberculosis by artificial pneumothorax it is well to realize that a potent and preventable cause of superimposed spontaneous pneumothorax is unphysiological pressure in the pleural cavity, by air, fluid or oil; too much air, too much oil, or neglected hydro-pneumothorax; and also that adhesions are a source of danger from tearing or giving away of a necrotic area at the base of an adhesion (McCloskey, 1937). Particular attention needs to be drawn to the fact that unphysiological pressure applies not only to excessive positive pressures, but also to excessive negative pressures. This is the reason why fluid or pus (from the development of a superimposed spontaneous pneumothorax) often develops in

an *abandoned* artificial pneumothorax. Those who permit an empyema to develop through neglect are as culpable as those who cause it through ignorance or carelessness. Once a physician has induced an artificial pneumothorax he is responsible for its proper maintenance or abandonment until complete re-expansion has taken place.

The complications of spontaneous pneumothorax are often serious in the course of pulmonary tuberculosis. The mortality is estimated at 16 to 25 per cent or more (Myers, Levine, and Leggett, 1937). While simple cases cause no undue concern, any case, even an early one, may prove to be a serious problem with a greatly altered prognosis, should spontaneous pneumothorax occur. Empyema, patent bronchopleural fistula, and congestive heart failure are most to be feared; mediastinal displacement may seriously embarrass a weakened heart or an already overburdened good lung; mediastinal hernia may make ineffective an hitherto effective pneumothorax; existing disease may be exaggerated.

The diagnosis of spontaneous pneumothorax is usually easy, but sometimes it is difficult. In the fluoroscope or the x-ray one looks for undue lung compression or mediastinal shift. The finding of a positive pressure in a previously negative-pressure pneumothorax denotes a closed spontaneous type (McCloskey, 1937). In the open valve type the manometric fluctuation (from a certain negative to a certain positive pressure) is constant even after removal of air. In the valvular type there is an increasing positive pressure not relieved by a deflation. The Coryllos school advocates examinations of the air of the pleural space (for percentage of oxygen and carbon dioxide) to diagnose small perforations, but this is usually not possible in India. Simpler, and quite sufficiently effective, methods to find a pleural perforation, in addition to those just mentioned, are: (1) injection of dye (2 c.cm. of 1 per cent watery solution of methylene blue) or a few drops of some aromatic oil (eucalyptus or peppermint) into the pleural space; or (2) putting a drop of the oil into the pneumothorax apparatus delivery tube: the odour is apparent very soon after introduction of scented air into the pleural space. (This method may not work when the perforation is submerged under fluid.)

*Physical examination.*—Dyspnoea may be quite evident—even when not complained of—and must always be explained. The signs in the chest are those of pneumothorax or of a hydro-pneumothorax. In tension pneumothorax there may be a lag in the movement of the involved side, obliteration of intercostal spaces, hyper-resonant percussion note, shifting in the position of the heart towards the normal lung, often to an extensive degree when the mediastinum is flexible. When the tear is patent and sufficiently large, amphoric breathing may be heard, or an amphoric echo with cough, or when fluid acts as

a valve over the rent (metallic tinkle). In severe collapse of the lung, producing bronchial closure, the breath sounds may be absent. As the lung re-expands amphoric breathing and other signs disappear.

*Treatment.*—In idiopathic spontaneous pneumothorax the chief treatment is rest in bed, with morphia for the pain and the dyspnoea. Deflation is necessary when the intra-pleural pressure is positive. For recurrences, it is wise to attempt a sealing of the pulmonary tear by intra-pleural injection of 25 to 50 c.cm. of 30 to 50 per cent dextrose to produce a sterile reaction (Brown, 1936; Young, 1936).

In tuberculous cases the first treatment is the immediate removal of sufficient air to relieve the dyspnoea or to save life. Oxygen will relieve the anoxemia if it is available. Collapse must be treated by the usual appropriate measures (heat, fluids, etc.), except that the Fowler head-up position is preferable to the head-down one on account of the dyspnoea. Morphia (in small doses) will help to calm the patient but large ones may obscure the anoxemia and permit relapse. It is absolutely essential to know whether the pneumothorax is increasing or not. In the continuous (open or valvular) types repeated or continuous aspiration of air must be arranged for. In less violent cases when the tear is apparently small it is wise to induce an effusion, if one has not already formed, by injection into the pleural space of dextrose (*see above*), or of oil (5 to 10 c.cm. of sterile olive or paraffin oil). An effusion should not be aspirated as it will aid in blocking the pulmonary tear; or if aspiration is indicated, as when the effusion is very large, only a small amount should be removed at one time, to relieve pressure.

It may be emphasized here that the onset of superimposed spontaneous pneumothorax by no means indicates that the pneumothorax is 'spoiled' and needs to be abandoned. Many cases recover and are none the worse for the accident, and may continue taking the treatment as before. On the other hand, in a larger number of cases the pneumothorax fails from this point of view, as the production of a pulmonary perforation sooner or later brings on empyema—tuberculous or mixed. Empyema so produced is a 'self-reinfecting empyema' and is the basic reason why simple aspiration, or aspiration *plus* antiseptic lavage so often fails. In these cases it is much wiser to abandon the pneumothorax treatment and accomplish both pulmonary collapse and empyema obliteration by thoracoplasty before the general condition of the patient worsens or a cross-spread into the good lung occurs. At the Wanless Sanatorium during the past two years this treatment (thoracoplasty) has saved every case in which it was possible to use it, while previously by 'medical treatment and aspirations' we lost every case.

We should not forget that certain cases of spontaneous pneumothorax respond favourably

to a phrenic interruption (a crushing is sufficient) when other measures fail.

An important item in the management of spontaneous pneumothorax is to have available at all times a suitable deflator. The books say 'insert a catheter into the pleural space' when the pulmonary tear is a large one, and let the end 'open slightly below the level of the patient into a weak antiseptic solution'. We have never done this. In tension pneumothorax it is necessary to relieve the positive pressure in the chest, and this can be accomplished by a simple automatic deflator as shown in figure 1. A needle is strapped to the chest wall under strict aseptic conditions, sealed in with benzoin and connected to this deflator. The illustration shows how the end of the tube is under water and the depth of the under-water exit can be adjusted to suit the need. This tube is also joined to the water manometer. This apparatus

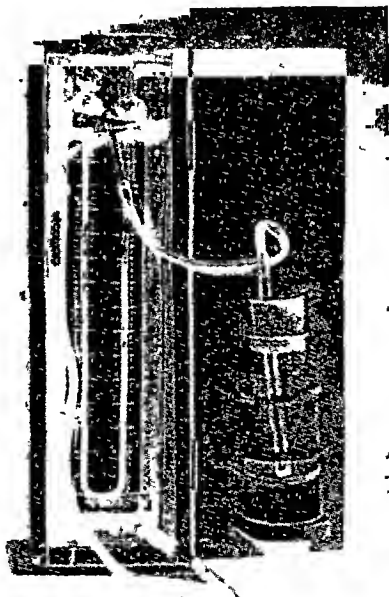


Fig. 1.

works well for a tension pneumothorax, but in our experience is not entirely satisfactory for routine use as it does not provide suction.

Hence we developed the continuous deflator shown in figure 2 several years ago, and it has proved its worth many times. While it appears rather complicated it is really a simple mechanism. We were given a pneumothorax apparatus now on sale in the U.S.A., consisting of a motor geared at right angles to a slow moving wheel on the periphery of which are six small rubber wheels. These rubber wheels run in a groove, compressing a rubber tube, thereby giving suction at the left end of the tube as indicated at 1. Suction is carried to the needle at 2, or *via* the bottle—for aspirating fluids—at 3. The degree of suction desired is regulated by a mercury escape valve 4. (The mechanism is simply that suction remains constant according to the depth of the hollow tube

under the mercury. A higher degree of suction draws in air from the outside through the hollow tube.) 5 is a safety valve in case of positive pressure, as from coughing, etc. The electric current from wall plug, 6, is carried through several electric light bulbs to supply resistance, as our motor is for 110 volts and our current 230 volts. Spare bulbs of varying wattage are carried in the box, 8, so that motor speed can be varied by changing the resistance. 9 is the off-and-on switch. 10 is the water manometer, made with an extra tube (a pipette) in the middle so that cough merely blows fluid from the left manometer arm into the pipette (as shown by the arrow), and the manometer arms are refilled to zero from this reservoir. The capacity of this aspirator is limited only by the excessive heating of the motor (due to improper voltages used) and by the motor speed which can be adjusted as described. Once in operation the patient or his attendants work the switch as needed. This saves the attending

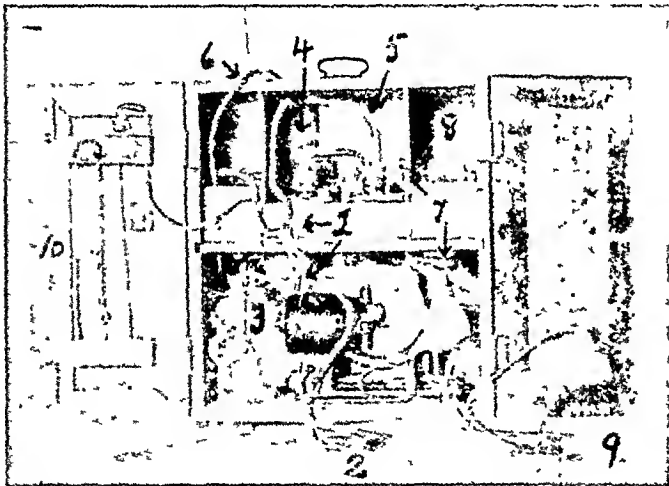


Fig. 2.—Electric decompressor (Wanless Sanatorium)

physician many an hour. Bottle 5 in this apparatus acts as a positive decompressor just like the one shown in figure 1.

#### Summary and conclusions

1. Spontaneous pneumothorax is a not uncommon accident in apparently healthy people, and these cases are found by using the x-ray freely in every kind of chest complaint. It is usually easy to treat, and complete recovery is the rule.

2. Spontaneous pneumothorax may also result from any kind of pulmonary disease that produces local necrosis of tissue. In tuberculosis it is quite common. It may be a serious complication and result in the death of the patient. It may come from extension of disease to the pleura; but in many instances it results from conditions which are under the control of the physician, and to this degree is preventable.

3. The treatment of spontaneous pneumothorax is often difficult and requires very prompt attention. A deflator and a continuous

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## TREATMENT OF TUBERCULOUS EMPYEMA

ILLUSTRATED REPORT ON 17 CASES TREATED IN THE  
WANLESS TUBERCULOSIS SANATORIUM,  
WANLESSWADI, DISTRICT SATARA

By G. SAMUEL, M.B., B.S. (Madras)  
Acting Medical Superintendent

A PURE tuberculous empyema is caused by the tubercle bacillus and a mixed tuberculous empyema is caused by the tubercle bacillus and pyogenic organisms. The latter is always due to superimposed infection either from within, i.e., from the blood stream, or from without, through bad technique during aspiration or from contiguous infection from the neighbouring organs. A broncho-pleural fistula or sometimes a spontaneous pneumothorax give rise to mixed infection.

A pure tuberculous empyema is caused by pleural tuberculosis or is secondary to a tuberculous lung infection. This is caused by discharge of infected material into the pleural cavity from any caseating sub-pleural tubercle on the surface of the lung, which commonly infects the benign effusion.

The inflammatory exudate or pus consists mainly of a dense network of fibrin in the meshes of which are serum and very large numbers of polymorphonuclear leucocytes. In the course of time, especially in long-standing empyema, the exudate is invaded by fibroblasts which lay down bundles of collagen fibres so that the affected portion of the lung is covered by a layer of exceedingly dense fibrous tissue: as the lung is encapsuled by a dense fibrous tissue wall the subsequent expansion of the lung is prevented, even after evacuating the pleural cavity. The parietal pleura becomes thicker by the same process and prevents the collapse of the chest wall after the thoracoplasty operation. This

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aspirator have been described. The treatment of the resulting bronchial fistula or empyema usually requires a thoracoplasty which gives excellent results in suitable cases.

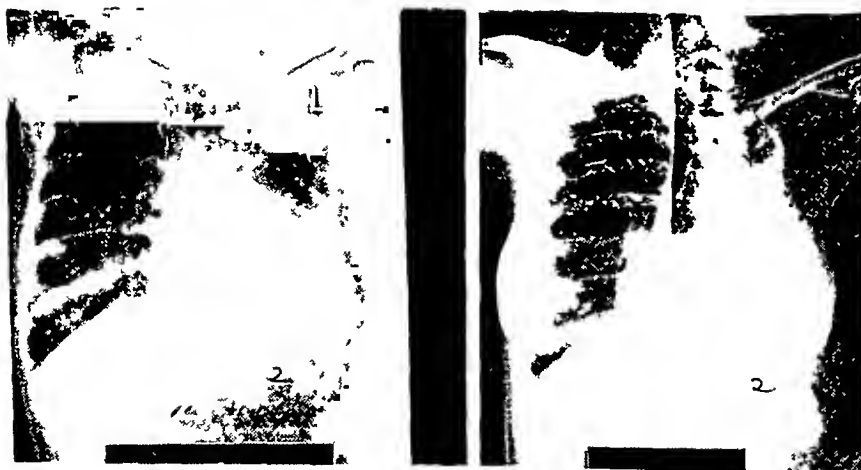
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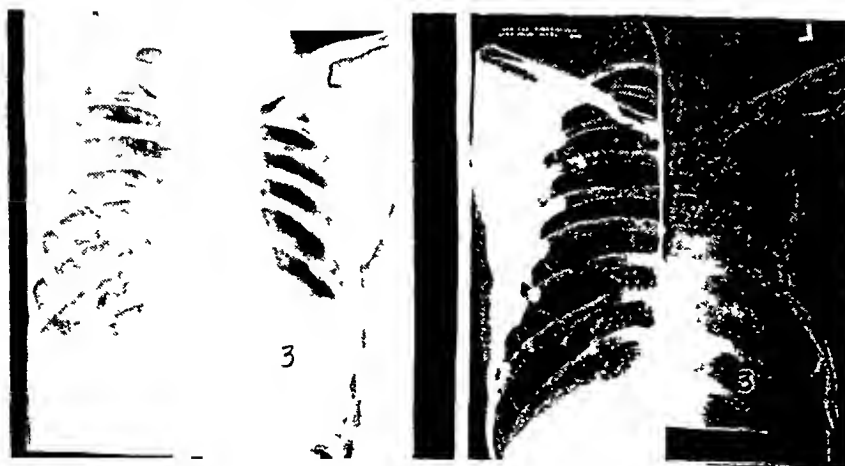
PLATE XVI  
TREATMENT OF TUBERCULOUS EMPYEMA SAMUEL



Case 1



Case 2



Case 3

PLATE XVII



Case 4.



Case 5



Case 6.



process affects the mediastinum also which is made stiff—a rigid wall is now interposed between the two pleural cavities. The effect on the lung of the purulent exudate is much more deleterious than on the visceral or parietal pleura. There may be necrosis and destruction of the lung tissue at the seat of pressure together with interstitial inflammation, which results in fibrosis and contraction and still further interferes with subsequent expansion.

About 4 to 5 per cent of all pneumothorax fluids terminate in tuberculous empyema, according to some authors, but much higher figures are sometimes given. The fluid in these cases becomes very thick and creamy and the smear often shows numerous tubercle bacilli.

If the empyema is left alone it may be recovered from spontaneously, provided it is of limited extent. It may kill the patient from septicaemia or amyloid disease, or the empyema may rupture externally or into neighbouring cavities such as a bronchus, the œsophagus or the peritoneal cavity.

#### *Classification of tuberculous empyema*

Hedblom's classification of tuberculous empyema into four groups is, in my opinion, the best one :

Group I.—Pure tuberculous empyema without pulmonary tuberculosis.

Group II.—Mixed tuberculous and pyogenic empyema without pulmonary tuberculosis.

Group III.—Pure tuberculous empyema with active pulmonary tuberculosis.

Group IV.—Mixed tuberculous and pyogenic empyema with active pulmonary tuberculosis.

#### *Indications for the treatment of tuberculous empyema*

1. If the underlying lung is tuberculous and requires thoracoplasty for itself, then the empyema (and the lung) should be treated by thoracoplasty.

2. If the underlying lung is not diseased or if it is tuberculous and for itself does not require thoracoplasty, the tuberculous empyema should not be treated by thoracoplasty unless aspiration treatment fails.

3. Thoracotomy should be used only when mixed infection exists and high toxæmia therefrom. It should then be done immediately.

#### *Aspiration treatment*

Aspiration once or twice weekly, with air replacement under negative pressure controlled by x-ray examination twice monthly, is advisable. Should any four consecutive films show no appreciable decrease in the pleural cavity, thoracoplasty should be done immediately.

Where thoracotomy and thoracoplasty are both indicated the thoracotomy should be done first, since the patient is thereby put in a much better condition to tolerate the thoracoplasty.

Thoracoplasty for tuberculous empyema is different from that done for pulmonary tuberculosis because :—

- (i) The patients are frequently much poorer risks for surgical shock,
- (ii) The collapse must be much more complete and calls for much more extensive decorticalization.

We divide the operation into 5 or 6 stages if necessary. We remove the full length of all ribs including the seventh; also in many cases the posterior half or two-thirds of the remaining ribs, exclusive of the twelfth rib. Ribs are removed extra-pleurally, beginning from above downwards. The periosteum of each rib is thoroughly treated with 10 per cent formalin throughout the entire length (instead of only in the posterior part, which is our custom in pulmonary tuberculosis). Sometimes extra-pleural thoracoplasty alone does not entirely obliterate the cavity, then Schade thoracoplasty has to be used for the treatment of the remaining cavity.

The records of the sanatorium contain 17 case reports of tuberculous empyema. Of these, 4 were treated with aspiration alone, 10 with thoracoplasty and 3 are still under treatment. It is too soon to report the results in the former; in the latter 8 cases (80 per cent) have obliterated cavities and completely healed wounds. The oldest cure has now been well for two years. One death occurred among the thoracoplasty group making a mortality of 20 per cent. The aspiration group shows no mortality.

Seven case reports with accompanying skiagrams are given as typical examples :—

*Case 1.*—Female, aged 30, was admitted on 3rd March, 1939—had a history of hæmoptysis in May 1930. Patient was apparently well but sputum-positive—x-ray showed a small cavity in the sub-clavicular region on the left side. She fell ill off and on during the period of six years. Artificial pneumothorax was started in December 1936. Sputum became negative for some time. Lung expanded owing to effusion—cavity re-opened; sputum became positive again. Had fever. Was aspirated off and on in a hospital in North India. Came here with tuberculous empyema with mixed infection and underlying lung disease. Thoracoplasty operation was undertaken on 7th March, 1939—four stages were done and the patient was discharged, with the empyema cavity obliterated, in a very good state of health.

(This case belongs to group IV.)

*Case 2.*—Female, aged 35, admitted here on 7th April, 1939—for tuberculous empyema with mixed infection due to underlying tuberculous lung disease—she developed pulmo-pleural fistula six years ago and was treated in other hospitals without effect. Productive cough—5 to 10 oz. of sputum every day; temperature up to 99.5°—anæmic—postural treatment and other medical and symptomatic treatment had no effect. Thoracoplasty operation was undertaken on 20th April, 1939—four stages were done. She is quite well with the empyema cavity obliterated.

(This case belongs to group IV.)

*Case 3.*—Male, aged 32, was admitted on 7th March, 1935, suffering from tuberculosis—left lung with a sub-clavicular cavity and caseo-pneumonic infiltration—sputum positive. Artificial pneumothorax treatment

was started and kept up for four months, when he developed effusion. Collapse was contra-selective because of apical adhesion. Internal pneumolysis was done—did well for two months with good collapse and sputum negative. Some time later the patient developed tuberculous empyema, several aspirations and irrigations of the pleural cavity were done but with no effect. Thoracoplasty operation was undertaken on 27th March, 1936. Two stages were done as the pocket was a small one. Patient was discharged quite well with the empyema cavity obliterated.

(This case belongs to group III.)

*Case 4.*—Female, aged 31, was admitted on 1st December, 1937, with caseo-pneumonic infiltration on the left side and multiple cavities—sputum positive. Artificial pneumothorax was started on 4th December. She had contra-selective collapse with some apical adhesions for which internal pneumolysis was done on 5th January, 1938. She had good collapse and was discharged with negative sputum on 14th October, 1938. Artificial pneumothorax was continued, but after some time she developed tuberculous empyema. She was readmitted in February 1939—several aspirations were done with no effect. Thoracoplasty operation was undertaken on 28th March, 1939—three stages were done—the pleural cavity was obliterated and the patient was discharged quite well.

(This case belongs to group III.)

obliterated. Patient was discharged on 14th October, 1937.

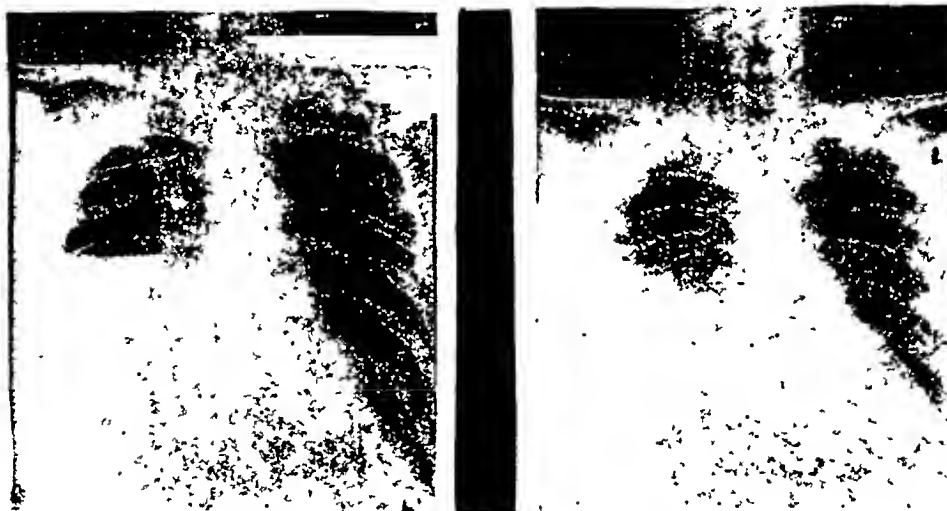
(This case belongs to group III.)

*Case 7.*—Male, aged 40, was admitted on 28th November, 1937, with caseo-pneumonic affection on the right side. Artificial pneumothorax was done and kept up for ten months with good collapse. Patient developed fluid on 19th May, 1938—fluid became turbid and became positive for tubercle bacilli—aspiration was started from 19th May, 1938, and kept up till 2nd December, 1938—twice weekly to begin with and once weekly later. The lung slowly expanded. The patient was discharged on 6th December, 1938, with sputum negative—the pleural cavity obliterated and the underlying lung disease controlled.

(This case belongs to group III.)

### Discussion

*Mortality.*—Our mortality figure, 20 per cent for treatment with thoracoplasty, is happily low. For example, recently Mattill and Jennings gave a mortality of 33½ per cent which is about the rate usually given. We ascribe our high survival rate to the early use of thoracoplasty and more especially to the use of many small



Case 7.

*Case 5.*—Male, aged 36, admitted on 31st May, 1938, with caseo-pneumonic infiltration on the left side with two sub-clavicular cavities—sputum positive. Artificial pneumothorax started on 3rd June, 1938—sputum became negative. As there was an adhesion, internal pneumolysis was done on 11th July with good collapse—sputum remained negative. After two months, in September 1938 effusion developed which became positive for tubercle bacilli. Aspirations were done for several months—the pus-pocket in the pleural cavity remained the same. Thoracoplasty operation was undertaken on 29th March, 1939—three stages were done and the pocket was closed. The patient was discharged quite well with pleural cavity obliterated.

(This case belongs to group III.)

*Case 6.*—Male, aged 20, was admitted for tuberculous empyema with underlying lung disease on 20th June, 1937. He had high fever and hacking cough—only two months' history. Heart was displaced and there was dyspnoea. Aspiration was done twice weekly and air put in under negative pressure. This treatment was continued from 23rd July to September 1937. The lung expanded and the underlying acute pneumonic infiltration disappeared and the pleural cavity became

stages in the operation. Delay and procrastination in applying radical measures cost human life, especially in mixed infection when the toxæmia rapidly lowers resistance (to surgical shock) by producing amyloid degenerative changes in the liver, kidneys and adrenal glands.

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## TUBERCULOSIS IN WOMEN: PREGNANCY AND TUBERCULOSIS

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IN Europe and North America, the problem of the tuberculous woman has been studied with increasing depth and scope continuously since the end of the great war, and it seems that any national programme of attack upon the disease must indisputably include among its major projects the sifting of data relating to tuberculosis as it bears upon the woman and her special physiology and domestic status.

The object of this paper is to trace some aspects of the problem, chiefly those relating to involvement of the female genital organs by the tuberculous process, the relationship to fertility, and the influence of pregnancy upon the course of the disease.

In India, the subject has already received attention in certain aspects. Muir (1926) reports that in 1922 in Calcutta, the death rate among women due to tuberculosis was 7.2 per thousand and mentions the drastic influences of early marriage and the purdah system upon the spread of tuberculosis among women in Bengal. These effects were deplored also by Shrikhande (1935) in relationship to pulmonary tuberculosis among women. Cases of uterine tuberculosis have been reported by Gupta (1928) and by Krishnaswamy, Goyle and Vasudevan (1936). Ukil (1930) puts the death rate of women between 15 to 20 years in Calcutta as six times greater than that of men. In a later paper, the same author (1933) presents the problem of the undiagnosed cases of tuberculosis among children under ten years and invites maternity and child-welfare clinics to utilize, for such cases coming to their notice, the facilities offered by tuberculosis dispensaries and clinics. Pai (1932) stresses the necessity of birth control and late marriage in tuberculous women. Riste (1938) in a review of deaths from tuberculosis occurring during a seven years' period in Ludhiana, Punjab, reports the female death rate as 2.7 times higher than that of males and attributes this high figure to early marriage, early child-bearing and purdah.

### *The effect of tuberculosis upon fertility in women*

In considering the influence of tuberculosis upon fertility in women, one is led to distinguish between actual attack upon the essential organs of reproduction—the uterus, ovaries and Fallopian tubes—and the effects upon them of the intoxication associated with attack upon other systems of the body (with which may be included vulvo-vaginal lesions).

#### *Group I*

*Attack upon the essential organs of reproduction.*—In this group two types of involvement may be envisaged: (1) mechanical interference

with the continuity of passages and destruction of the tissues by the tuberculous process, such as occur in salpingitis, oöphoritis, cervicitis and endometritis; and (2) pathological changes of non-specific character such as sclero-cystic disease of the ovaries (the *tuberculoase inflammatoire* of Poncet and Leriche, 1910), a condition almost invariably detected in animals dead of tuberculosis, and probably a reactive rather than tuberculous manifestation.

#### *Group II*

*Ovarian dysfunction arising from tuberculous intoxication.*—The second group is composed of conditions or symptoms suggestive of, or referable to, ovarian dysfunction, or upset of the sex hormone system—symptoms such as dysmenorrhœa, amenorrhœa and other disturbances of menstruation including delayed puberty.

It is generally accepted, although one must admit that few studies on really assessable lines have been recorded, that where the organs of reproduction are not the site of attack, in the earlier age groups at least, the fertility of tuberculous women is little, if any, less than that of their non-affected sisters.

Jameson (1935) states that at Saranac one or more pregnancies among tuberculous married women was twice as common as sterility.

Skillen and Bogen (1938) in connection with a review of 10,000 patients of the Olive View Sanatorium, California, state that one-fifth of the married women patients had never been pregnant, 718 out of 2,633 had not been delivered of a live child, while one-third of those who had had pregnancies, had only one child. The average number of children in this group was 2.2.

Gow (1940) refers to the greater fertility of tuberculous women in Bengal when compared to the non-tuberculous.

All such statements and figures have, however, to be considered in the light of many factors—the degree to which contraceptive measures are employed, the age groups in question, the activity and nature of the tuberculous disease, the presence of co-existing venereal infections of the genital tract likely to affect fertility, the fertility of the non-tuberculous ascertained on strictly comparable lines and finally, and not least important, the attitude towards pregnancy in the tuberculous, maintained by eminent local phthisiologists and obstetricians. In the United States, for example, Trembley's (1909) views were responsible for widely held medical opinion in favour of termination of pregnancy.

*Extent of genital involvement.*—Although in the majority of cases genital lesions are secondary to infection elsewhere in the body, primary genital attack of every type occurs. Regarding Indian cases, Gupta describes two cervical out of six genital cases as primary, while in none was pulmonary involvement present when the genital lesions were investigated. On the other

hand, in five out of eight cases recorded by Krishnaswamy, Goyle and Vasudevan, the pelvic lesions appear to have been secondary to pulmonary lesions.

With regard to secondary genital attack, the figures of Merletti (1901) are of interest. At autopsy upon 1,350 women dead of pulmonary tuberculosis, this author detected genital lesions in 172 cases (12.6 per cent). Jameson, after careful examination of the pelvic organs at autopsy upon 17 women dead of tuberculosis, detected genital involvement in six (35 per cent). Bouilly advises extirpation of the tubes and ovaries in all instances of laparotomy performed for abdominal tuberculosis, as he is convinced that the abdominal condition is secondary to invasion of the tubes.

The attack upon the pelvic organs in generalized disease must of course be considered separately. Hirsch and Hoffmann (1933) report that during an immunization programme at Lübeck, in the case of 11 infants accidentally infected through food, all of whom died of generalized tuberculosis, nine showed genital lesions of which five, only, were tubal.

*Age in relationship to genital tuberculosis.*—It must be borne in mind that although genital attack may be manifest at any age (in Askanasy's case, cited by Daniels, uterine tuberculosis occurred in a child of 2½ years) the greatest incidence occurs during the early child-bearing period.

The ages of Gupta's six patients are given as 21 years, 34 years in three cases, 30 years, and 40 years, while the ages of Krishnaswamy, Goyle and Vasudevan's cases are given as 20 years in two cases, 23 years, 25 years in three cases, 26 years, and 32 years.

### Group I

#### *Tuberculous genital involvement*

*Tuberculous salpingitis.*—In considering the first group one has to admit that the most frank evidence in favour of sterility must be related to the proportionate number of tubal infections. In at least 75 per cent of cases of tuberculous salpingitis, the attack is bilateral, commonly with early involvement of the ampulla. Conception in such cases is almost precluded, although ectopic gestation in a tuberculous tube has been reported by Wetterdal (1924) and 17 cases collected by him from the literature.

Excluding cases of involvement other than pelvoperitoneal, Jameson in an analysis of 73 cases of salpingitis, from the literature, obtained the following figures:—sterile 17 per cent, pregnancies 16 per cent; for 37 cases seen by himself, however, the returns were 85.6 per cent sterile and 14.2 per cent in whom pregnancy occurred. Greenberg (1921) gives 63.5 per cent as the sterility rate and Bush (1933) 61 per cent. The figures in all cases refer to married women only and are not discussed with reference to sterility in non-tuberculous women.

*Frequency of occurrence.*—The figures cited by various authors vary from 50 per cent or less to over 90 per cent, but microscopic examination of the tissues has usually been omitted by those authors giving low percentages. As regards Indian records, although Gupta states that, if the uterus is attacked, the tubes are always involved, and that salpingitis is the commonest genital lesion, in only one case out of six reported by him, and that one in which the uterus also was attacked, is tubal infection mentioned as present. In three out of eight cases reported by Krishnaswamy, Goyle and Vasudevan, salpingitis was present. One must, however, bear in mind that microscopic section requires to be resorted to before infection of the tubes can be eliminated.

It is a significant fact also that the peak incidence of tuberculosis of the Fallopian tubes appears to lie between the second and third decades, the richest reproductive period.

*Tuberculous oöphoritis.*—Ovarian involvement offers a less well-defined and probably underestimated relationship to sterility in the tuberculous woman. Although in approximately 25 per cent of all cases of tuberculous salpingitis the ovaries are involved by direct extension, forming a tubo-ovarian mass, destructive lesions of the ovary are rare, and even then may be unilateral, the other ovary proving unaffected or showing a reactive change only. Primary lesions of the ovary although very rare do occur, but even assuming, somewhat exaggeratedly, that tuberculous salpingitis forms 90 per cent of genital tuberculous lesions, the occurrence of frank disease in the ovary probably would not be met with in excess of 25 per cent of all genital cases.

In the investigation of fertility, weight is being given increasingly to the non-specific changes in the ovary met with in tuberculous women, changes such as sclero-cystic disease resulting in ovarian dysfunction. Poncet and Leriche believe that this condition is an inflammatory form of tuberculosis which may be lit up at any time by strain (as may occur during delivery or the puerperium), a view which has not received general support.

*Tuberculous cervicitis and endometritis.*—Although authors variously assess uterine involvement at 12 per cent—76 per cent, Norris (1921) and others state that in about 50 per cent of all cases of genital tuberculosis in women, the uterus is attacked. There is some evidence that cervicitis is commoner than is usually stated, and occurs earlier than infection of the endometrium. In the case reported by Gipel, salpingitis, endometritis and cervicitis occurred in an infant of six months. Gow, referring to Bengal, puts the incidence of tuberculosis of the cervix uteri at 1 in 605 and asserts that young girls are more frequently the victims of this manifestation. Of the six cases of uterine involvement discussed by Gupta, four were cervical

and in one more the cervix fundus and tubes were all infected. Krishnaswamy, Goyle and Vasudevan's eight cases included five in which the disease was located in the cervix.

Tuberculous endometritis arises as a rule in the functionalis layer and can be diagnosed by premenstrual curetting only, as the diseased endometrium is at first shed with the menstrual flow. Vogt (1928) doing diagnostic curettage for sterility found tuberculous endometritis existed in only 7.2 per cent of 212 cases.

It would appear therefore that the relationship of uterine tuberculosis to sterility is not a highly significant one. Deymel (1927) and Gupta each report a case of multiple pregnancy in a woman with long-standing uterine infection. Of the five additional cases reported by Gupta one patient is described as sterile, two were multiparæ and in two instances pregnancy is not mentioned. Regarding Krishnaswamy, Goyle and Vasudevan's eight patients, no mention is made of children in three cases, one is described as a nullipara, two had had one child, one had had five, and one three children.

*Non-specific lesions of the ovary.*—Jameson describing studies related to the examination (post-mortem) of the internal genital organs of 14 women between the ages of 30 to 40 years, in all of whom pulmonary tuberculosis had been the cause of death and none of whom had exhibited gross evidence of genital invasion, states that the ovaries were normal in size, cystic changes were present in nine, while in all the tunica albuginea showed definite thickening.

Such tunical thickening, although not pathognomonic of tuberculosis, is bound to affect ovulation adversely. This author further remarks that on the analogy that deficiency of follicular hormone is indicated by atrophic endometrium a study of uterine curettings of tuberculous women pointed to a deficiency of ovarian secretion in the majority.

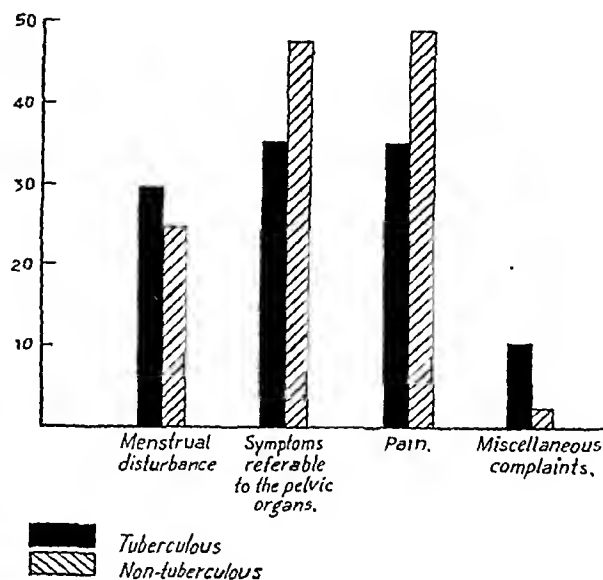
There is no doubt that sclero-cystic changes in the ovaries are very much commoner in tuberculous than in non-tuberculous women. Jameson states that this change is almost invariably present with or without the presence of other genital lesions.

The microscopic appearance of the organ in this condition—thickened and adherent tunica, a considerable increase of the stromal substance at the expense of the epithelium, and the preponderance of cystic and atresic follicles—suggests that although probably in the early years fertility is little interfered with, even in the tuberculous women in whom no specific genital lesion occurs, the period of fertility may conceivably be shortened.

#### Group II

*Ovarian dysfunction resulting from tuberculous intoxication.*—Amenorrhœa, with which is also classified scanty menses, is taken as direct evidence of interference with the full functioning

of the ovaries, while menorrhagia and hypermenorrhœa are considered the effect of dysfunction *plus* the result of loss of capillary tension which is the normal accompaniment of menstruation.



Nomogram comparing the gynecological complaints of 122 tuberculous and 139 non-tuberculous women (studied by Jameson).

[Figures taken from *Gynecological and Obstetrical Tuberculosis*, Jameson, 1935.]

The nomogram is compiled from the figures given by Jameson relating to the gynecological complaints of a group of 122 tuberculous women, compared with those of 139 non-infected. It will be seen that menstrual disturbances attain a slightly higher figure, 29.2 per cent in the former group, as against 24.6 per cent in the non-tuberculous group. The chief forms of disturbance are dysmenorrhœa, metrorrhagia, menorrhagia and scanty flow.

Stanitch (1923) emphasizes that the ovaries are among the first organs to be affected by the intoxication of acute generalized tuberculosis, the signal of such attack being either amenorrhœa of abrupt onset or menorrhagia with increased flow and a shortened intermenstrual interval. It is well known that compromise of the defence mechanism in tuberculosis in women is frequently indicated by marked menstrual disturbance, either in the form of amenorrhœa or of menorrhagia of a severe type. Stanitch regards amenorrhœa as a valuable guide to the allergic condition of the patient. Certainly in fibroid phthisis the menses are seldom abnormal. Macht (1910), classifying scanty menses with complete amenorrhœa, found that in 27.3 per cent of all tuberculous women patients seen such disturbance occurred, and that 71.5 per cent of these patients were under 30 years of age. Morris gives the high figure of 77 per cent of women patients as having suffered from menstrual disturbance of some type. In none



of these patients were clinical manifestations of pelvic infection present.

*Delayed puberty.*—The more chronic forms of tuberculosis in the young, *e.g.*, Pott's disease, recurrent pleurisy, scrofula, etc., are often associated with delayed puberty. Stanitch reports puberty occurring at 16 to 20 years in such cases and points out that menstruation, when established, has no apparent deleterious effect upon the lesions.

*Menstrual irregularities.*—Haese (1927) upon analysis of 469 patients with a normal menstrual cycle states that ultimately irregularity of amenorrhœa occurred in 17.4 per cent. This author found that using the N. T. A. (U. S. A.) standards, irregularity of menstruation was twice as common in the second stage of infection as in the first, although the proportion of amenorrhœa was slightly less. In the third stage, with cavitation, irregularity occurred twice as frequently as in the second stage, while the proportion of patients with amenorrhœa was nearly four times as high as in stage 1 (11.1 per cent). Haese does not consider that dysmenorrhœa bears any significant relationship to tuberculosis. Jameson's figures also are of interest: in 20 per cent of 200 cases, a history of irregularity or amenorrhœa prior to diagnosis of the disease was elicited. Subsequent to diagnosis this figure rose to 26 per cent, although the extent of the disease process seemed to have little influence on menstruation.

Friedrich (1913) cites the highest figures of all. This author records 45 per cent amenorrhœa in stage 1, 64 per cent in stage 2, and 85 per cent in stage 3.

There seems little doubt that menstrual irregularity is manifest in a considerable proportion of women patients, irrespective of the site of lesion. Its significance as an indication of the progress of the disease and the extent of ovarian disturbance is not clear. Certainly under treatment some patients resort to a regular cycle. That menstrual disturbance has an evil effect upon the course of the tuberculous condition is however generally accepted; probably both are simultaneous manifestations of a failure of defence. In India figures are not forthcoming relating to the frequency and clinical significance of menstrual disturbance in tuberculous women, although much valuable data must be recorded in women's hospitals and in the gynaecological departments of the large teaching hospitals.

#### *Pregnancy and tuberculosis*

Subsequent to 1918, with the establishment of improved methods of diagnosis of tuberculosis, clearer light has been thrown upon the inter-related factors, which bear upon this common combination of a physiological and pathological disturbance of metabolism and much has been added to the literature on the subject in recent years.

In assessing the effect of pregnancy upon the tuberculous, one must distinguish between the

effects of the pregnant state, the strain of delivery and the significance of the puerperium.

Although several authors have written of the influence of pregnancy upon the higher incidence of tuberculosis among women, the figures of Brindeau (1931) and Bridgman and Norwood (1926) dealing with 32,667 and 14,000 pregnant women, respectively, show no evidence of a higher incidence among parturients.

It is true that in India certain factors peculiar to the country's social structure require to be assessed in this regard, before the figures of France and the U. S. A. can be deemed applicable here, but this very social structure, producing as it does groups distinct ideologically, may offer thereby the greatest facility for the elucidation of special problems, if opportunities were forthcoming.

It is obvious that if the strain of early puberty is shortly followed by the strain of a first pregnancy, capacity to resist infection is bound to be reduced. Thus in India it is necessary to estimate the several effects upon the incidence of tuberculosis in women, of pregnancy at an early age (*e.g.*, delivery before the age of 16 years), of repeated pregnancies at short intervals, and of such factors favourable to infection as lack of sunlight, unsuitable or poor diet, inadequate rest and medical care.

Although it has not been possible to trace any study made in this country designed to elicit, by reference to strictly comparable control groups, information regarding the influence of such factors, certain authors such as Pai, Shrikhande and Riste have referred to the subject. Pai mentions the value of birth control and late marriage in the control of tuberculosis, while Shrikhande also stresses the evil effects of purdah and early marriage upon pulmonary tuberculosis. Riste, taking the mortality rates of seven consecutive years in Ludhiana, Punjab, ascribes the higher rate among women (2.7 times the mortality rate of males) to early marriage, early child-bearing and purdah.

It is clear that much more requires to be known about the influence of these factors under Indian conditions.

Certain conclusions reached at the Obstetrical and Gynaecological Congress held in Geneva in 1923 (Morisson-Lacombe, 1924) are of interest as indicating the first swing away from the two divergent, largely uncompromising schools of thought then existing, the one regarding pregnancy as favourable, the other as disastrous, to the course of the disease in the tuberculous woman. Aggravation of the lesions, to the extent of about 60 per cent, was held to occur, by predominant opinion at the congress, such aggravation increasing as term approaches. It was emphasized that each case should be observed by an obstetrician and phthisiologist, *while greater weight should be given to the opinion of the latter*. Although it was considered better for the tuberculous woman to avoid pregnancy, the necessity to distinguish the patient



with the long healed fibrous lesion from that with active disease was stressed, provided always that strict medical supervision could be maintained throughout pregnancy and afterwards.

Induction of abortion later than at the third month was deemed dangerous, and in this regard the congress elicited certain facts upon which decision might be taken regarding the advisability of induction when pregnancy is detected before the end of the third month. These were termed 'signs of gravity' and 'signs of alarm'.

Briefly, in regard to the 'signs of gravity' the congress found that benign fibrous lesions and pleurisies are little affected by pregnancy, serious results being unlikely to occur in more than 5 per cent of cases. Progressive fibro-caseous lesions on the other hand were held to be aggravated in almost all cases, afebrile patients with active non-progressive disease or chronic cavities being excepted.

Tuberculosis becoming manifest clinically for the first time during pregnancy was held to deserve special consideration, as being more dangerous owing to the possibility of tuberculous pneumonia supervening. Special significance, it was noted, should be ascribed to the development of complications peculiar to pregnancy.

'Signs of alarm' referred to clinical and other evidence of aggravation of the disease, including changes in allergy as demonstrable by cutaneous reactions.

Since 1923, investigation of the problem both experimentally in animals and by observation of patients has tended to strengthen the position of those who maintain that after certain data (similar to those suggested at the Geneva Congress) have been collected and weighed, any decision for or against artificial termination of pregnancy must take into account personal factors, and conditions in India demand that personal factors should include the economic status, the domestic responsibilities and the capacity for co-operation of the patient. The available facilities for adequate observation and treatment must finally influence the decision. In spite of this there are authors who believe with Bourne (1931) that artificial abortion has no place generally in the treatment of tuberculosis. Gow (1940), on the other hand, with regard to Bengali women considers interference advisable as late as the 28th week of pregnancy. It seems highly important that obstetricians and phthisiologists in this country should combine to elicit data on which procedure might to some extent be standardized, all the more as in the majority of the smaller hospitals and to many practitioners by whom such decisions are being taken, the opinion of a specialist in tuberculosis is seldom available. It is true that we do not face a falling birth rate, as Germany did when her obstetricians were being influenced in favour of conservation of pregnancy but if, as many authors state, to bring about termination of pregnancy after the third month has a more

deleterious effect upon the patient than continuation of pregnancy to term, should we not know whether or not, conditions as they exist socially in India to-day, cancel in effect the balance in favour of conservation?

Of the few statistical studies made upon this subject that of Hill (1928), comparing the condition of 160 women (in whom pregnancy accompanied or immediately preceded the disease) with their state one year and two years after diagnosis of the disease or of conception or parturition (according to the group), yielded most interesting evidence.

No appreciable effect of pregnancy upon the progress of the disease was elicited. It was found that the earlier the diagnosis of pregnancy, the safer was the pregnancy, for the women: less than one-twelfth only of the women diagnosed before gestation were dead a year after termination of pregnancy: of those diagnosed during pregnancy, one-fifth, and in the case of those diagnosed after delivery, the high figure of one-third. Hill states that as in the case of primiparae in general, among the tuberculous the highest mortality rate was suffered by those pregnant for the first time.

The importance of this problem to the phthisiologist is reflected in the fact that Hill found that the maternal mortality rates of tuberculous mothers correspond with the deaths at different ages of all tuberculous women.

*Effects of pregnancy.*—The work of Abruzzese (1929) has shown that probably in the tuberculous patient the change most to be feared in pregnancy is that increased capillary permeability, which attains a maximum about the seventh month, after which time it decreases to rise again for a few days in the early post-partum period. The part played in the exacerbation of lesions by decalcification, hyper-cholestræmia and endocrine readjustment in pregnancy is not clear. In regard to hormones, the work of Steinbach and Klein (1937) has shown that antuitrin S has a favourable effect upon the tuberculous lesions in animals; Skillen and Bogen, on the other hand, report that neither follicular nor corpus luteum hormones appeared to influence the course of the disease in animals.

The question of pregnancy in tuberculosis cannot be considered apart from the facilities for adequate and efficient amelioration of the disease during the period of pregnancy and for at least six months subsequent to delivery; the value of artificial pneumothorax, etc., in suitable cases need not be stressed here. Such operative aids must also have the buttress of willing and intelligent co-operation of patient and relatives alike, while for those for whom the tedium of enforced rest of minimal activity must be the prescribed course how enormous must be the contribution in patience and faith made by the patient.

*Spontaneous abortion in tuberculous women.*—Russi (1926), reviewing 75 patients of whom three-quarters were sick enough to require

hospitalization before delivery, found that 41 per cent had premature labours, 50 per cent went to term, 9 per cent had abortions. In the case of patients with the disease first diagnosed or appearing during pregnancy, 29 per cent only went to term, while 35 per cent had premature labour. As regards obstetrical intervention, the amount resorted to corresponded to that in non-tuberculous patients. Jameson reports that in his experience of a few cases, all women went to term.

#### *Conduction of labour in the tuberculous woman*

There is one point which seems to have been overlooked in the consideration given to the question of the delivery of the tuberculous woman in this country, namely, the presence of an obstetrician at delivery and facilities for the application of anæsthesia.

Sodium amytal, morphine, even forceps in the second stage of labour, skilful nitrous oxide and oxygen anæsthesia are favoured by modern workers. In fact any method of delivery designed to reduce shock, limit muscular strain, and control hæmorrhage is necessarily that most favourable to the tuberculous patient. Care during pregnancy may be largely countered by labour unskilfully conducted, followed by exhaustion.

In India even in large towns there is often the greatest difficulty in obtaining an ante-natal bed for the tuberculous woman in our overcrowded hospitals and maternity institutions, because of the natural fear of spread of infection in general wards. Sanatoria are few and often too far distant.

Admission during labour and discharge after ten days is all that in most cases can be achieved. Under such conditions pregnancy is bound to take a heavy toll. Ante-natal beds for tuberculous patients are an imperative need in any maternity hospital. The services of an honorary phthisiologist for all such institutions is also highly desirable.

One would again suggest that it is to the phthisiologist that the problem must be presented, and with him must be aligned, as Ukil has suggested, the maternity and child-welfare clinics and facilities for institutionalization for ante-natal care and delivery. The pregnant woman who is infected with tuberculosis, once she has made a contact with any part of the system, should be able to obtain treatment for the disease throughout the pregnancy, and be ensured delivery conducted under the most favourable conditions, with her child and herself coming under care from the puerperium onwards. If the units in the system are dissociated, the result is not only disastrous to the woman and discouraging to the clinician, but dangerous also to the child, who has not therefore been isolated from the mother.

The present social conditions in this country make it difficult for the system of treatment in sanatoria to be linked closely with maternity hospitals and institutions and it may be that in

order to achieve reliable data on a subject of really vital importance at least one sanatorium project in India should make provision for the tuberculous pregnant woman throughout pregnancy, during delivery and from the puerperium onwards.

The control of such patients in the home can only be tackled with hope of success when the functions of the generalized health visitor have been realized and the problem of her training and her linking to institutions which serve the pregnant and the tuberculous woman has been adequately achieved.

Further, the co-operation of the general practitioner requires to be enlisted in order to effect some attempt at standardization. The issue of uniform record forms to be filled in by him for each tuberculous married woman coming under his care may well be undertaken by the Tuberculosis Association, the completed card being returned to the Association, for record of data.

Such measures have been undertaken in the United States and have proved most useful.

#### *Summary*

Two forms of tuberculous attack seem likely to affect appreciably the fertility of women of child-bearing age, tuberculous salpingitis and secondary, toxic (sclero-cystic) changes in the ovaries, the latter met with frequently in tuberculous disease although not pathognomic of such.

It is not clear to what extent the menstrual irregularity, which features in a considerable proportion of tuberculous women, is significant as an indication of the progress of the disease and the extent of ovarian disturbance.

The importance of considering separately the effects of pregnancy, delivery, and the puerperium upon the course of the disease is stressed.

A study to assess the influence of pregnancy and parturition upon the tuberculous woman with special reference to factors such as early puberty, early and frequent child-bearing, unsatisfactory diet, inadequate rest and medical care, is urgently needed. A sanatorium project, with this aim, improved control of patients in the homes by development of the system of care by the generalized health visitor, and standardized reports by private practitioners are suggested as possible approaches to the problem.

As a tuberculous pregnant woman should be under the care of a phthisiologist throughout pregnancy and for six months after delivery, the provision of ante-natal beds for tuberculous women in maternity hospitals and the appointment of honorary phthisiologists to such institutions is suggested. It is pointed out that delivery in every case should be undertaken by an obstetrician having at his disposal efficient medical resources to reduce muscular strain, shock and hæmorrhage, and to arrange for the protection of the infant from infection by the mother.

(Continued at foot of opposite page)

## DIET IN TUBERCULOSIS

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THE importance of nutrition in the production and course of tuberculosis has long been recognized in medicine. Deficiency of nutrition is

(Continued from previous page)

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regarded as one of the predisposing causes of tuberculosis and the disease itself is characterized by considerable wasting of the tissues. Proper feeding, therefore, plays an important rôle both in prophylaxis and treatment of tuberculosis. 'Good food' is one of the fundamental items of our present-day sanatorium regime. But although the need of supplying proper nourishment is generally accepted, there has been much controversy in recent times as to the quantity and nature of foodstuffs required. Hippocrates about 400 B.C. advocated a milk diet when there was no high fever and barley water and honey for febrile states, whereas John Mirfield in A.D. 1400 put forward the claims of 'river crab and sugar of roses'.

*Overfeeding :—Old and modern views*

In the earlier period of sanatorium treatment Otto Walther of Nordach preached and practised 'stuffing' of his patients with as much food as they could be made to take. He taught his patients to eat whatever was put before them irrespective of their appetite, taste and state of digestion. If the patients vomited, they had to start all over again. One of the enthusiasts (Debove) went so far as to introduce food through the stomach tube. In other words, overfeeding was regarded as a 'cure' and the patients were made to swallow food like medicine.

The idea of 'food cure' which held sway for a considerable time was gradually given up. It was later found that the rapid and excessive gain in weight which followed forced feeding did not help in increasing resistance or combating tuberculous toxemia; nor did it enhance the process of cicatrization of lesions. On the other hand, the overload of useless fat and water greatly undermines the general health. The patient is weak, flabby and breathless with rapid pulse; his appetite and digestion are impaired and in some cases the digestive mechanism is so upset that the patient loses in a few days what he had gained in several months.

It is now customary to take a more rational view. We now recognize that the progressive increase of weight is not an index of improvement unless it is also accompanied by amelioration of symptoms and unless physical signs and x-ray examinations show evidence of healing. Consistent with these improvements, we aim at a slow and persistent gain finally reaching 10 to 15 lbs. higher than the patient's normal weight in health.

*Adequate and balanced dietary*

(a) *Caloric value.*—What is required is not overfeeding but an adequate and balanced diet. Bardswell and Chapman (1908) after a thorough experimental study of the subject concluded that 3,000 calories per day are quite sufficient. The figures published by the League of Nations and the British Medical Association corroborate Bardswell and Chapman's standard. The

average Indian patient will require a little less but a patient who will not improve with 3,000 calories will not do so with any amount of stuffing.

(b) *Proteins*.—Besides the requisite caloric value, the food must contain all the proximate principles—protein, fat, carbohydrate and vitamins in proper proportions. As tuberculosis is associated with considerable wasting of protein elements, the natural tendency was to make good this loss by feeding on excess of protein food. Some advocated animal proteins while others preferred vegetable proteins. In France, eating of raw meat (zomotherapy) was in vogue. Proteins, however, are said to increase the respiratory activity, and, as fats and carbohydrates are known to be protein-sparers, this has been used as an argument against excessive meat eating.

In India where the people are mainly vegetarian, milk is the chief source of protein. Non-vegetarians may make a wide choice from goat, mutton, game and poultry. In Bengal, fish supplies a cheap source of easily assimilable proteins.

(c) *Fats*.—The one advantage of fat is that, unlike protein and carbohydrate, it does not materially increase the volume of respiration or metabolism. But an excess of fat inhibits gastric secretion and is not well borne by most patients. Apart from its inherent vitamin content, fat by itself does not possess any specific healing power. Feeding on excess of fat should therefore be discouraged. Of all fats, butter is most liked by patients and is easily digested. Ghee and vegetable oils, which are used for cooking, are good vehicles for supplying fat, besides making the food more appetizing.

(d) *Carbohydrates*.—As for carbohydrates, we take more rather than less of it. Patients on high-carbohydrate and low-fat diet put on more weight than those on high-fat diet. As carbohydrates spare both protein and fats, they play an important part in body building.

(e) *Vitamins*.—Vitamins A and D are credited with having the power of increasing resistance against tuberculous infection. They are derived from the fatty food contained in a balanced dietary, and it is customary to prescribe these in excess in the shape of cod-liver oil, adexolin, haliverol, etc. Recently Abbasy, Harris and Ellman (1937) have shown that patients with active tuberculosis must take much more anti-scorbutic vitamin (vitamin C) than normal individuals before it can be detected in their urine.

Two oranges a day or their equivalent amount of dry ascorbic acid (vitamin C) are worth while adding to the dietaries.

(f) *Minerals*.—Cereals combined with green vegetables and fruits supply all the mineral salts required.

*Condiments*.—These are best left to individual taste. In institutions, however, where diverse tastes are to be catered for, they

should be sparingly used. What is appetizing and palatable to one will be too hot and rich for another. Besides, an excess of condiments is apt to upset digestion.

(h) *Milk and eggs*.—We take the opportunity of saying a few words on these two articles of food because of the advice freely given to the consumptives 'drink plenty of milk', 'eat plenty of eggs'.

Milk is certainly a perfect food in the sense that in addition to containing all the proximate principles in proper proportions it is rich in mineral salts and vitamins. A quart of milk is equivalent in food value to a pound of lean meat or 8 eggs. It appears to be the ideal food for growing infants in dilutions suited to their relatively large stomachs. But for adults its bulk is too much for the digestive organs to handle easily. In our experience many patients, who drink a lot of milk for a quick cure, develop flatulent dyspepsia and diarrhoea. We must, therefore, prescribe just as much milk as they can easily digest. In our hospital we used to give 1 seer of milk daily. By cutting it down to  $\frac{3}{4}$  seer of milk and  $\frac{1}{2}$  pow of *dahi*, indigestion of our patients has been diminished.

Eggs are very hard to digest specially when they are taken raw. They should always be taken fried, scrambled or boiled. As eggs do not stimulate gastric juice and resist tryptic digestion, they should never be prescribed for patients with weak digestion. For Indian patients, not more than 2 eggs a day should be prescribed. Many cases of colicky pains and diarrhoea may be traced to eggs.

(h) *Variety*.—From what I have said, it is apparent that a good diet should be a mixed diet containing a variety of all elements and not a preponderance of one element or the other. It should be changed from meal to meal and day to day to prevent monotony. What is even more important is to see that the food is properly cooked and artistically served. The dishes should be spotlessly clean, and the food should look appetizing and attractive. Dettweiler who made a great success with his sanatorium used to say that his kitchen was his pharmacy.

#### *The daily menu*

A fixed weekly menu in an institution is better avoided, although it has many advantages from the administrative point of view. Patients will in such cases forecast the next day's menu and they will be anything but pleased when their forecast comes true.

As regards the number of meals, some experts recommend 5 to 7 meals or more a day which means that the patients would be eating and drinking almost throughout the day. Small frequent meals will not give the stomach and intestines the required rest and is sure to spoil the appetite. We prefer to give 4 meals a day—two principal meals at 11 a.m. and 7 p.m.—

one good meal at 7 a.m. and a light meal at 4 p.m.

At least half an hour's rest before each meal is of great importance. This improves the appetite. Smoking before meals causes temporary hyperglycæmia and spoils the appetite. If allowed, it should be advised after meals.

Fluids should be taken in between the meals and not with them; lemonade makes a good stimulating beverage.

The following is our daily menu for full diet for Indian patients :—

7 a.m.—Buttered toast; half-boiled, scrambled or poached egg; dalia or oatmeal porridge; milk.

11 a.m.—Rice, vegetables curried or boiled; dāl; meat curry or stew; chutney; *dahi*; lemon.

4 p.m.—Milk; fruit; sweets.

7 p.m.—Rice, chapati or luchi; vegetables fried or curried; dāl; fish curry; milk.

The following list shows the quantity of raw foodstuffs supplied per patient per day :—

Rice and atta .. 12 oz.	<i>Dahi</i> .. 4 oz.	Potatoes .. 6 oz.
Dāl .. 2 "	Egg .. One	Green vegetables 8 "
Meat .. 4 "	Fruit .. One	Sugar .. 2 "
Fish .. 2 "	item	Lemon .. One
Bread .. 3 "	Butter .. $\frac{1}{2}$ oz.	Salt and condi- ments as required.
Milk .. 24 "	Ghee .. 1 "	
	Mustard oil 2 "	

The diet, as set forth above, contains approximately 125 gm. of protein, 130 gm. of fat and 470 gm. of carbohydrate and yields about 3,500 calories. The above calculations are based on the quantities of crude foodstuffs and, allowing 500 calories for preparation and cooking, the diet gives about 3,000 calories which is the standard requirement. The cost, excluding the pay of the cook, comes to about 12 annas per head per day.

#### *Personal and economic factors*

Unlike many Indian sanatoria, we supply food to all our patients. The advantage is that the patient's diet is entirely under our supervision and control and the patients are saved a lot of worry and bother. Whereas there is much to recommend in this system, we must not forget that there is nothing like a standard diet in this country which will suit the needs of all individuals. The nature of foods and the modes of cooking are as diverse as are the habits and customs of the people. They vary from province to province, district to district and no two households are alike in this respect. A patient who has been brought up on a particular kind of dietary and has developed his likes and dislikes will find it difficult to adapt himself to the standard menu and if he is sentimental, as many tuberculous patients are, he is sure to react by anorexia and digestive disturbances. In Bengal the diet is more homogeneous than in other provinces, and still we find it impossible to

cater for all tastes. In view of this difficulty, we are now building a few cottages with attached kitchens, where the patients will have facilities to cook for themselves.

Economic factors should also be taken into consideration. Tuberculosis is more prevalent among the poor, who are underfed in the normal circumstances of life. It is a disease which inflicts prolonged suffering and the unfortunate patients who, deprived of earning capacity, has often to depend, with his family, on the charity of others. To give him an impression that only 'plenty of eggs and milk' can cure him is to make him pessimistic about his future and drive him to desperation.

The question of prescribing a diet is, therefore, more or less an individual problem. The diet must be designed so as to suit the individual palate, the purse and the needs of the patients, remembering that tuberculosis requires just a little more food than is required for a healthy person. In private houses such individualization of diet is quite easy but in institutions it is more difficult. Here we have to think of the community which the institution mainly serves. For example, Frimley Sanatorium, which is under control of the Brompton Hospital, London, is principally meant for working-class people and their diet consists of the ordinary food that the people of this class can provide for themselves. The diet of Jadabpur is quite suitable for middle class Bengalees from whom the majority of our patients are derived. A common labourer placed on this diet will gain in weight rapidly, only to lose as rapidly when he returns to his home conditions.

#### *Diet in other Indian sanatoria*

With a view to ascertaining how the problem of diet is met in other Indian sanatoria and special hospitals, we sent out a questionnaire to the heads of 23 tuberculosis institutions. Unfortunately, only 5 replies were received. We give below in tabular form a summary of the relevant portions of the information received, including our own.

#### *Special forms of diet*

Although there is no specific diet for tuberculosis, experts have from time to time put forward special dietetic formulæ claiming for these remarkable therapeutic properties. We shall only mention two of these :—

(a) *Gerson's salt-free diet*.—Gerson of Germany, supported by Sauerbruch, has devised a new diet the principles of which are based on the 're-mineralization' theory and consist in—

(i) Elimination of 'common salt and addition of 'mineralogen' which is a mixture of many mineral salts, except chlorides.

(ii) Limitation of carbohydrates.

(iii) Diminution of animal proteins.

(iv) Use of vegetables and fruits in excess.



The majority of observers have failed to reproduce the good results claimed by its sponsors and at present the consensus of opinion is that the cost and the trouble are not worth undertaking, at least for pulmonary tuberculosis.

(b) *High caloric diet with insulin*.—Recently Vere Pearson and Day (Rolleston and Moncrieff, 1939) have advocated what they call 'high

8-15 p.m. followed in half an hour each time by 6 ounces of fruit drink (made of orange, lemon juice and sugar). During treatment the patients should have lumps of sugar or glucose drink handy so that on the slightest manifestation of hypoglycæmia (cold sweat, tremor, sinking feeling) they may help themselves and avert alarming symptoms.

Name of the institution	Percentage of patients who are supplied food from the Sanatorium kitchen	Number of meals per day	Nature of diet	Caloric value	Cost per patient per month	Opinion as to whether food should be supplied from the institution
Hill-side Sanatorium, Vengurla, Bombay.	50	5	Mixed diet suitable for rice eaters.	3,000	Rs. 15	Not necessarily. Cooking according to patients' liking but under medical supervision.
Royapetta Hospital, Madras City, and Tambaran Sanatorium, Madras.	100	6	Mixed diet specially suitable for South India.	..	15 to 20	The patients should be encouraged to have their own diet. Only milk, eggs and cunji to be supplied from the sanatorium.
Visrantipuram Sanatorium, Rajahmundry, Madras.	85	5	Do.	3,000	10	Sanatorium diet for those who cannot afford their own. Others to arrange according to their liking but under medical supervision.
S. J., T. B. Hospital, Delhi.	100	4	Mixed diet suitable for Indians.	..	30	The food should always be supplied by the sanatorium except in special cases.
Bel-air Sanatorium, Panchgani.	100	6	Mixed diet mainly European.	..	30	The food should be supplied from the sanatorium although the task is difficult. There are different cooks to cater for different communities.
Jadabpur T. B. Hospital.	98	4	(a) Indian diet specially suitable for Bengalees. (b) Mixed diet cooked differently for Anglo-Indian patients.	3,500	23 27	Yes, but the patients who cannot adapt themselves to hospital diet should be given facilities to cater for themselves under supervision.

caloric diet' combined with insulin. The underlying principle is to give carbohydrate in excess which helps in body building and in the language of the authors 'seems to coincide with a decreased destructiveness of the diseased process as witnessed by the decline of the sedimentation rate'. Insulin is combined 'to give the victim a real famished feeling' and to increase his carbohydrate intake.

The diet gives 4,000 calories and consists in giving extra dishes of carbohydrate preparations with the usual English lunch, tea and supper into the details of which I need not enter. Sixty units of insulin are given in 24 hours in 6 injections of 10 units. Three of the injections are given 20 to 30 minutes before the principal meals (8-30 a.m., 1-15 p.m., and 7 p.m.). The other 3 are given at 11 a.m., 1-45 p.m., and

The method is worth giving a trial in selected cases where the patients can afford it and are not putting on weight or gaining strength under the usual regimen. Half a dozen injections daily with risks of hypoglycæmia and insulin-sensitization render this method unsuitable for use in a mass scale.

#### *Diet in complications*

(i) *In hæmoptysis*.—Where the sputum is only streaked with blood or the hæmoptysis is slight, a little curtailment of the diet is all that is necessary. When the bleeding is active and severe, all solids should be withheld and all feeds should be served cold. Milk diet (2 to 3 pints a day) is usually recommended, but as pure milk does not agree with most patients it may

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## A PSEUDO-TUBERCULOUS CONDITION ASSOCIATED WITH EOSINOPHILIA

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### Introduction

AMONG many patients sent to the Union Mission Tuberculosis Sanatorium, Arogyavaram, diagnosed as having tuberculosis on account of

(Continued from previous page)

conveniently be mixed with barley water or fruit juice, or served as ice cream. Gelatin given in the form of jelly is supposed to increase the coagulability of the blood and will be welcomed by many fastidious patients. Twenty-four hours after the bleeding has stopped pudding and porridge may be given even if the patient is bringing up clots. Resumption of ordinary diet should not be too long delayed, as absence of proper nourishment will only help in the spread of the disease.

(ii) *In tuberculous enteritis*.—A pure milk diet is recommended by some, but as milk does not agree with most of these patients it is better avoided. Dry milk preparations are, however, digested by many. Milk may also be given as *dahi* beaten up with water into a drink. Sometimes proprietary milk foods like Horlick's malted milk are better tolerated.

To avoid irritation of the ulcers, roughage should be reduced to a minimum. Strained vegetable soup and mashed potatoes serve the purpose well. We combine this with soft rice and lean fish. In no case should vegetable or fruit pips be allowed to be swallowed.

All experts agree in giving a high calcium and high vitamin diet. Food calcium is supplemented by calcium injections. Two ounces of orange juice with  $\frac{1}{2}$  ounce of cod-liver oil or a few drops of adexolin or haliverol should be given 3 or 4 times daily. When oranges are not available tomatoes may be substituted.

(iii) *Laryngeal tuberculosis*.—Special dieting is called for only when there is dysphagia. When this condition develops, the throat should be anaesthetized with cocaine or orthoform before giving foods. When dysphagia is at all severe, pasty, semi-solid foods like porridge or pudding are swallowed with greater ease than either solids or liquids.

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the usual clinical symptoms associated with the disease, we find an increasing number who, after a thorough examination, we are convinced have no tuberculosis at all. In many of these patients a skiagram taken when the patient has first consulted his doctor has apparently confirmed the diagnosis even to the point of signifying advanced disease.

In this paper we wish to call attention to a group of these patients where we think an error of diagnosis has been made chiefly on the interpretation of the *x*-ray picture. With the more frequent use of *x*-rays in the diagnosis of chest conditions, there is the possibility of a greater number of these people being wrongly condemned as tuberculous, a mistake we ourselves made in the earlier years of our work.

The first indication that we were facing what may be called a pseudo-tuberculous condition arose out of routine blood examinations of all our patients. Some of these showed a very high eosinophile count, even to over 90 per cent in the differential count. Very few of these had tubercle bacilli in the sputum, even when in more recent years we have used culture methods and stomach-wash examinations for the isolation of tubercle bacilli. These patients had almost all the usual symptoms of tuberculosis including fever, cough, sputum, loss of weight, chest pain and sometimes hæmoptysis, and by physical examination showed the signs usually taken as indicating tuberculosis. At the same time we began to notice that in many of these patients the skiagrams showed a fairly constant similarity. The condition is so typical that in the common parlance of our *x*-ray room it is called 'eosinophile lung'. This is characterized generally by an extensive mottling over both lung fields, usually evenly distributed; the size of the shadows is about 2 mm. and there is usually a certain amount of increased striation. In some patients the *x*-ray findings are more marked than in others. The general appearance is something similar to miliary tuberculosis or to silicosis.

Since we began to think these cases might not be tuberculous, we have done tuberculin reactions, and the majority of these have been negative. We have also studied changes in the differential count after subcutaneous injections of 'old tuberculin', and in most there was no increase in the *stabkernige* cells, a strong indication of the absence of an active tuberculous condition.

A further study of this condition showed that these patients had a good prognosis as judged by the discharge results and after-histories, beyond what could have been expected had the condition been tuberculous.

It has also been possible to check up some of these patients several years later, and they have still shown the same condition, especially in the *x*-ray picture and the blood picture, and sometimes also the clinical symptoms were unchanged.

*Material selected for study*

In selecting material for this study we went through our records since 1925, when routine blood studies were first begun in the institution and about which time also the x-rays began to be used, and we selected all patients, who on admission had an eosinophilia higher than 20 per cent. We also included 179 patients since 1930, (when routine monthly blood studies began) who, although coming with less than 20 per cent eosinophiles, had above that figure during their stay in the sanatorium. This made a total of 533 patients, out of about 5,500 admitted during the period reviewed. Besides these, we have also included 67 patients who came for consultation without being admitted, and who had above 20 per cent eosinophiles or more, making a total of 600 altogether for review.

The figure of 20 per cent eosinophiles was chosen as the lower limit, partly because it was indisputably a high eosinophilia, even though eosinophilia is common in India where helminthiasis and skin infection are frequently found, partly because we have not found those with below 20 per cent eosinophiles showing the x-ray picture referred to above.

*General review of material*

The records of the 600 patients were first analysed according to eosinophile count, sputum

possible, about the aetiology of the condition which we are studying.

The arrangement in the tables is according to absolute eosinophile count as being more accurate than the percentage of eosinophiles in the differential count, although in practical work we find this percentage gives sufficient information. There are included in the tables those patients, 179 in number, who were admitted with less than 20 per cent eosinophiles, but who had an eosinophile count above that figure during their treatment, all with less than 1,000 eosinophiles, and the majority of those with between 1,000 and 2,000 eosinophiles were admitted with less than 20 per cent. In the majority of these there was a transient eosinophilia which could be explained without reference to any lung condition. An increase in eosinophiles is fairly frequently seen during or soon after treatment with sanocrysin, an observation of Houghton (1932) and others. Attacks of unexplained pruritis, eczematous skin conditions, scabies, exacerbation of filarial infection also caused eosinophilia during treatment.

The highest eosinophile counts met with were 85,000, 48,160, 47,880, and 42,390 per c. mm. The highest eosinophile percentage was 92 per cent.

From table I it will be seen that 194 (32.3 per cent) of the patients had tubercle bacilli and so were definitely tuberculous. With the increase

TABLE I

*Sputum and stool examinations in 600 patients with an eosinophile percentage of 20 or more on admission or during treatment*

Eosinophile count on admission (per c.mm.)	Number of patients	TUBERCLE BACILLI IN SPUTUM		STOOL EXAMINATIONS				
		Number	Per cent	Number examined	Ova found	<i>E. histolytica</i> and/or <i>Giardia</i>	Number with intestinal infection	Percentage with intestinal infection
0-500 ..	44	39	88.6	43	26	1	26	60.5
500-1,000 ..	59	45	76.3	59	38	2	40	67.8
1,000-2,000 ..	103	42	40.8	101	78	11	80	70.9
2,000-3,000 ..	66	26	39.4	65	42	7	44	67.7
3,000-5,000 ..	45	15	33.3	42	28	4	30	71.4
5,000-10,000 ..	72	6	8.5	72	42	10	47	65.3
10,000-20,000 ..	74	3	4.1	72	23	11	28	38.9
Above 20,000 ..	18	2	11.1	18	9	2	9	50.0
No absolute count	119	16	13.4	37*	22	3	25	67.6
TOTAL	600	194	32.3	509	308	51	329	64.6

\* The stools of patients coming for consultation were not examined.

examination for tubercle bacilli, stool examination for ova and for cysts.

These findings are given in table I.

In a number of patients with sputum negative for tubercle bacilli, tuberculin tests were done and the results are shown in table II.

The classifications in tables I and II were selected with a view to obtaining information, if

of the eosinophile percentage, the percentage of positive sputum findings rapidly decreases; e.g., below 2,000 eosinophiles, 126 out of 206 (61.2 per cent) have tubercle bacilli; above 5,000 eosinophiles, only 11 out of 164 (6.7 per cent) have tubercle bacilli.

The number of patients with ova is high, namely 308 out of 509 examined (60.5 per cent).

TABLE II

Reaction to tuberculin of tubercle bacilli negative patients with an eosinophile percentage of 20 or more on admission or during treatment

Eosinophile count on admission (per c.mm.)	Number showing no tubercle bacilli	Number examined with tuberculin	PIRQUET OR MANTOUX		OLD TUBERCULIN AND SCHILLING		NEGATIVE TO TUBERCULIN	
			-	+	-	+	Number	Per cent
0-500 ..	5	4	1	3	0	2	0	0.0
500-1,000 ..	14	13	5	6	2	2	5	38.5
1,000-2,000 ..	61	31	13	13	13	8	15	48.4
2,000-3,000 ..	40	19	11	6	9	6	11	47.5
3,000-5,000 ..	30	20	11	7	11	4	12	60.0
5,000-10,000 ..	66	35	20	11	23	3	23	65.7
10,000-20,000 ..	71	40	22	14	24	4	25	62.5
Above 20,000 ..	16	3	3	0	1	0	3	100.0
No absolute count	103	23	14	4	9	1	18	78.3
TOTAL ..	406	188	100	64	92	30	112	59.6

Of these patients we found that 250 (49.1 per cent) had hookworm infection, and 58 other helminth infections without hookworm, mostly *Ascaris lumbricoides* and *Trichuris trichiura*. The helminthiasis is higher than the general average, for another examination of 3,000 patients showed only 28 per cent infected with hookworm.

From table II it may be seen that of 406 patients who showed no tubercle bacilli, 188 were examined with tuberculin, 164 with von Pirquet or Mantoux, and 122 with old tuberculin followed by the Schilling count. As stated earlier, tuberculin was not used much in the earlier part of the period under review.

The von Pirquet test was done with undiluted old tuberculin and the Mantoux generally with a standard dilution of 0.1 c.cm. of 1/1,000, but, in a few patients 0.1 c.cm. of 1/10,000 was used, and in some the standard dilution, if negative, was followed by 0.1 c.cm. of 1/100. In the old tuberculin test with the Schilling count, 0.3 c.cm. of 1/100 old tuberculin was given subcutaneously, with Schilling counts on each of two days

before, and 24 hours and 48 hours after the injection. The technique is described by Benjamin and Barton (1937).

It will be noted that of the 188 patients examined with tuberculin, 112 (59.6 per cent) were negative. As there was no reason to suppose these patients were in an anergic condition, this is strong evidence of the absence of tuberculous infection. Although the figures are small, there is indication that, the higher the eosinophile count is, the more numerous are tuberculin-negatives.

#### Study of the x-ray

The next part of the investigation was a study of the skiagrams. This was possible in 430 of the 600 patients with high eosinophilia. In 170 no x-ray film was available for study, because in some of the earliest of the series of patients no skiagram was taken, in some patients coming for consultation screening only was done, in earlier years some films were sent away with the patients, and some of the early films were not satisfactory for the present study.

TABLE III

Examination of x-ray films of patients with high eosinophilia

Eosinophile count on admission (per c.mm.)	Number of patient-	TB-positive patients with 'non-eosinophile lungs'	TB-NEGATIVE PATIENTS	
			'Non-eosinophile lungs'	'Eosinophile lungs'
0-500 ..	41	39	2	0
500-1,000 ..	58	43	8	7
1,000-2,000 ..	89	39	33	17
2,000-3,000 ..	49	24	15	10
3,000-5,000 ..	37	9	10	18
5,000-10,000 ..	52	4	12	36
10,000-20,000 ..	45	0	4	41
Above 20,000 ..	7	0	0	7
No absolute count	52	2	11	39
TOTAL ..	430	160	95	175

Out of the 430 patients, 175 gave an 'eosinophile lung' x-ray picture, as described earlier. All had a negative sputum. In none of the bacilli-positive cases was there a typical 'eosinophile lung' picture; 95 patients were negative for tubercle bacilli in the sputum and had no 'eosinophile lung' picture (table III).

From table III it will be seen that the 'eosinophile lung' picture was more often found in patients with the higher eosinophile counts; of 102 patients with a count of over 5,000 eosinophiles, 84 had the characteristic x-ray findings, while of 266 patients with below 5,000 eosinophiles, only 52 had the characteristic x-ray. The positive sputum findings decrease with the increase of eosinophiles.

The 'eosinophile lung' picture varied considerably in degree, being very marked in some individuals and only of slight degree in others, the variation not always connected with the number of eosinophiles.

Consideration of 175 'eosinophile lung' patients

If we consider the 175 patients whose x-ray showed the characteristic picture, we find the following :—

(a) Sex and age distribution

Age	Men	Women
Below 10 .. ..	6	2
11-15 .. ..	13	6
16-20 .. ..	30	9
21-25 .. ..	35	9
26-30 .. ..	31	4
31-35 .. ..	12	3
36-40 .. ..	9	3
41-50 .. ..	3	..
TOTAL .. ..	139	36

The proportion of men to women is slightly higher than that for all patients admitted to the sanatorium, being about 4.1 against the average of about 5.2.

The age distribution is largely the same as that found for all patients admitted to the sanatorium, the only point being that there are

rather more in the youngest age group and no old people are found.

(b) Symptoms and physical findings

If we consider the symptoms as given in the patients' histories, or on examination in the sanatorium, we find the following the most common :—

Cough .. ..	153
Fever (history) .. ..	144
Sputum .. ..	110
Loss of weight .. ..	86
Pain in chest .. ..	84
Coloured sputum or hæmoptysis .. ..	45
Asthma or bronchitis .. ..	35
Loss of strength .. ..	31

A history of influenza or pneumonia was given by 28 patients.

On physical examination, 91 patients had râles or rhonchi; 63 of 146 patients admitted had fever, mostly low, for a very short time after admission.

From the above figures, it will be seen that it was quite natural that the patients were sent here with a diagnosis of tuberculosis.

(c) Stools

The stool findings are shown in table IV.

From table IV it will be seen that there is a lower incidence of intestinal infection than is found for the whole group of 600 patients as shown in table I, 48.2 per cent as against 64.6 per cent in the large group. Also the percentage of patients with the eosinophile count over 5,000 is less than those with a count of under 5,000, namely 40.2 per cent, as compared with 56.9 per cent.

Tuberculin tests

Of the 175 'eosinophile lung' patients, 106 were tested with tuberculin, and the reactions are shown in table V.

In table V it will be seen that 74 (69.8 per cent) were negative to tuberculin; there being no appreciable difference between those with above 5,000 eosinophiles and those with below 5,000. The percentage of negative reactors is

TABLE IV  
Stool examinations of tubercle bacilli negative patients and 'eosinophile lung' x-ray findings

Eosinophile count on admission (per c.mm.)	Number of patients	STOOL EXAMINATIONS				
		Number examined	Ova found	<i>E. histolytica</i> and/or <i>Giardia</i>	Number with intestinal infection	Per cent with intestinal infection
500-1,000 ..	7	7	4	0	4	56.9
1,000-2,000 ..	17	17	11	1	11	
2,000-3,000 ..	10	9	6	1	6	
3,000-5,000 ..	18	18	8	0	8	
5,000-10,000 ..	36	35	17	4	19	40.2
10,000-20,000 ..	41	40	11	4	12	
Above 20,000 ..	7	7	2	0	2	
No absolute count	39	8	6	0	6	..
TOTAL ..	175	141	65	10	68	48.2

higher than in the whole group of patients with negative sputum, as shown in table I, where the percentage is 59.6.

*Present condition.*—Very similar to last examination; general condition good. Physical findings showed again numerous rhonchi and fine râles over all lung fields. Temperature 100°F. (evening rectal) for three days.

TABLE V

*Tuberculin reactions in tubercle bacilli negative patients with 'eosinophile lung' x-ray findings*

Eosinophile count on admission (per c.mm.)	Number of patients	Number tested with tuberculin	PIRQUET OR MANTOUX		OLD TUBERCULIN AND SCHILLING		TUBERCULIN NEGATIVE	
			—	+	—	+	Number	Per cent
500-1,000 ..	7	7	1	4	6	1	3	70.3
1,000-2,000 ..	17	12	7	2	8	1	9	
2,000-3,000 ..	10	7	6	1	3	1	6	
3,000-5,000 ..	18	11	8	4	9	2	8	
5,000-10,000 ..	36	27	16	7	20	3	19	68.4
10,000-20,000 ..	41	28	15	10	22	2	18	
Above 20,000 ..	7	2	2	0	1	0	2	
No absolute count	39	12	7	3	6	1	9	..
TOTAL ..	175	106	62	31	75	11	74	69.8

*Illustrative case histories*

(i) K. S., 13 year old boy.  
*First admission* from 18th September, 1932, to 6th December, 1932.  
*Family history.*—An older brother, a patient in the sanatorium in 1927, diagnosed non-tuberculous, with high eosinophilia.  
*Previous history.*—Cough on and off for five years; last four months increased cough with much sputum.  
*Physical examination.*—General condition fairly good. Auscultation showed râles and rhonchi all over both lungs. Other organs nothing special. Temperature normal.  
*X-ray.*—Over whole of both lung fields an evenly distributed mottling of small shadows, non-confluent, about milary size, with increased striation all over (figure 1).  
*Sputum.*—Twelve direct smears and one concentration negative for tubercle bacilli.  
*Blood.*—Hæmoglobin 95 per cent; red cells 4,376,000; leucocytes 19,000; neutrophils 29 per cent (*Stabkernige* 1.5); eosinophiles 52 per cent; basophile 1 per cent; lymphocytes 17 per cent; monocytes 1 per cent; sedimentation rate 39 mm. (Westergren 1 hour); Kahn +; malaria parasites not found.  
*Stools.*—No ova or cysts found.  
*Weight.*—66 lb., increasing to 80.  
The patient improved well under symptomatic treatment.  
*Second admission* from 29th May, 1936, to 3rd August, 1936.  
*History.*—For 2½ years after discharge remained well, then again cough and little sputum, with short period of fever; a local hospital reported a few acid-fast bacilli in antiformin smear.

*X-ray.*—As previously, extensive mottling over both lungs, a little more intense on right side, but of same type as reported above. No changes suggesting exudative lesion (figures 2 and 3).  
*Sputum.*—Twelve direct smears, three concentration tests and one culture, all negative for tubercle bacilli.  
*Blood.*—Hæmoglobin 85 per cent; red cells 4,584,000; leucocytes 16,000; neutrophils 17 per cent (*Stabkernige* 1.0 per cent); eosinophiles 63.5 per cent; basophiles 0 per cent; lymphocytes 13.5 per cent; monocytes 6 per cent; sedimentation rate 58 mm. (Westergren 1 hour); Kahn ++ (no clinical symptoms of syphilis).  
*Stools.*—Hookworm ova present; no amœbæ or cysts found. No bacilli found (three direct smears).  
*Tuberculin.*—von Pirquet—positive.  
*Weight.*—Increased from 97 to 101 lb.  
The patient improved again under symptomatic treatment.  
(ii) Male, age 27. Admitted 21st May, 1936; discharged 9th June, 1936.  
*Family history.*—Nil.  
*Previous history.*—1934 high fever for two months; last three months cough, fever, little sputum.  
*Physical examination.*—General condition good; auscultation showed some fine râles over right lung only. Temperature 99.8°F. (evening, rectal).  
*X-ray.*—Both lung fields show extensive mottling of numerous small non-confluent nodules, not very sharply outlined, about milary size, evenly distributed over whole field; increased fine linear markings, some striations leading upward to apices from hilus (figures 4 and 5).  
*Sputum.*—Four direct smears and one concentration negative for tubercle bacilli.  
*Blood.*—Hæmoglobin 85 per cent; red cells 4,944,000; no malaria parasites; Kahn negative.

*Counts*

Date	W.B.C	Total neut.	Stab.	Segment.	Eos.	Baso.	Lymph.	Mono.	Eosin. myelocytes	ESR mm., 1 hour
11-5-36	28,720	19.0	5.5	13.5	64.0	0.0	14.5	2.5	..	98
1-6-36	..	27.75	8.0	19.75	47.25	0.0	22.5	2.0	0.5	
2-6-36	*	20.75	10.0	10.75	55.25	0.0	19.5	3.75	0.75	
3-6-36	..	20.5	8.5	12.0	66.25	0.0	12.25	0.25	0.75	
4-6-36	..	22.75	6.5	16.25	57.5	0.5	15.5	2.75	1.0	

\* Old tuberculin 3 mg. given subcutaneously on 2nd June, 1936.

*Stools.*—No ova or cysts found; no tubercle bacilli found (four direct smears).

*Tuberculin.*—von Pirquet negative; old tuberculin and Schilling count negative (*see above table*) with no local or general reaction to 3 mg. of old tuberculin subcutaneously.

*Weight.*—Increased from 108 to 110 lb.

(iii) Male, age 18. Admitted 21st November, 1936; discharged 13th February, 1937.

*Family history.*—Nil.

*Previous history.*—Many attacks of fever in 1935. thought to be malaria; dry cough and low fever last four months with little sputum; loss of weight 12 lb.

*Physical examination.*—General condition good; auscultation showed no râles or rhonchi; later few rhonchi found. Temperature 100°F. (evening, rectal).

*X-ray.*—Both lung fields show more than normal lung markings, mostly due to increase of linear striations, and also numerous miliary-sized opacities, not confluent (figures 6 and 7).

*Sputum.*—Thirteen direct smears and two concentrations and one culture (six tubes) negative for tubercle bacilli.

*Blood.*—Hæmoglobin 116 per cent; red cells 5,664,000; no malaria parasites found; Kahn negative.

demonstrate tubercle bacilli, and a high percentage of the cases are tuberculin negative.

In 113 of the 175 patients, a Kahn test was done, and was positive in 15, which is a higher percentage, being nearly double that found in the routine examination of our patients. None of the patients, however, showed clinical manifestations of syphilis, and the x-ray picture is not that usually associated with a syphilitic lung, nor is eosinophilia a characteristic finding in syphilis.

Pneumoconiosis is another possibility that has to be considered. The usual industrial pneumoconiosis, such as silicosis, anthracosis and asbestiosis, can be ruled out in our series of patients as they were not engaged in such dusty occupations. If the lung condition were due to the ordinary dust of a dusty country, the condition should be extremely common in many parts of

### Counts

Date	W.B.C.	Total neut.	Stab.	Segment.	Eos.	Baso.	Lymph.	Mono.	Eosin. myelocyte	ESR, mm., 1 hour
23-11-36	13,800	28.5	4.0	24.5	57.5	0.0	13.0	1.0	..	10
30-11-36	..	18.5	6.25	12.0	68.25	0.25	10.5	2.75	..	..
1-12-36	*	26.5	4.75	21.75	57.5	0.0	12.25	3.75	..	..
2-12-36	..	18.0	5.25	12.75	63.0	0.25	14.25	4.25	0.25	..
3-12-36	..	20.0	6.0	14.0	61.5	0.25	15.0	3.25	..	..
18-1-37	..	9.0	3.5	5.5	61.0	0.5	27.5	2.0	..	17

\* Old tuberculin 3 mg. given subcutaneously on 1st December, 1936.

*Stools.*—Trichuris ova found; no cysts.

*Urine.*—Occasionally albumin +, with few casts and pus cells. No tubercle bacilli found.

*Tuberculin.*—von Pirquet negative; old tuberculin and Schilling count negative (*see above table*), with no local or general reaction to 3 mg. of old tuberculin subcutaneously.

*Weight.*—Increased from 105 to 118 lb.

### Discussion

The above three case histories make it clear that we have to deal with a lung condition which cannot easily be classified under the most common chronic lung affections.

In none of the x-ray films of the special group of 175 were typical tuberculous changes manifest, such as early or advanced infiltrations, of either exudative or more productive character and which, if found, are mostly confined to certain areas of the lung. The only form of tuberculosis with which this appearance could be compared would be that with either a hæmatogenous or bronchogenic dissemination of tubercles all over the lungs. But in these 'eosinophile lung' cases the elements in the lung condition have a smaller appearance than is generally found in the different forms of miliary tuberculosis, and linear markings are more increased than even in chronic miliary tuberculosis. Besides the nature of the x-ray findings not being quite typical, we have shown that in none of the cases have we been able to

India, but there is no evidence of this. Normally eosinophilia is not noted as being associated with pneumoconiosis. Also the usual x-ray picture found in persons affected by dusts normally shows much more linear marking than in our cases. However, further studies are needed before ordinary dust can be ruled out as an agent.

Chronic changes in the lungs due to long-standing heart disease can be ruled out as a cause, because in only one patient was valvular disease noted.

Another lung condition associated with eosinophilia is Löffler's syndrome (Löffler, 1932). But this is a fleeting infiltration with eosinophilia, which appears suddenly and disappears within a fortnight. It appears in certain localized areas of the lung and leaves no trace on resolution. In none of our cases have we found any changes of this nature and in most of them the lesions have shown no marked changes in the time we have observed them, and in several we have even found the same change after several years.

In connection with Löffler's syndrome it has been suggested, for example by Wild and Loertscher (1934) and Müller (1938), that the x-ray changes in the lung are caused by the passage of ascaris larvæ through the lungs. Müller was able to produce in himself fleeting multiple infiltrates in the lung with eosinophilia, by eating



PLATE XVIII  
A PSEUDO-TUBERCULOUS CONDITION ASSOCIATED WITH EOSINOPHILIA



Fig. 1. Case 1.

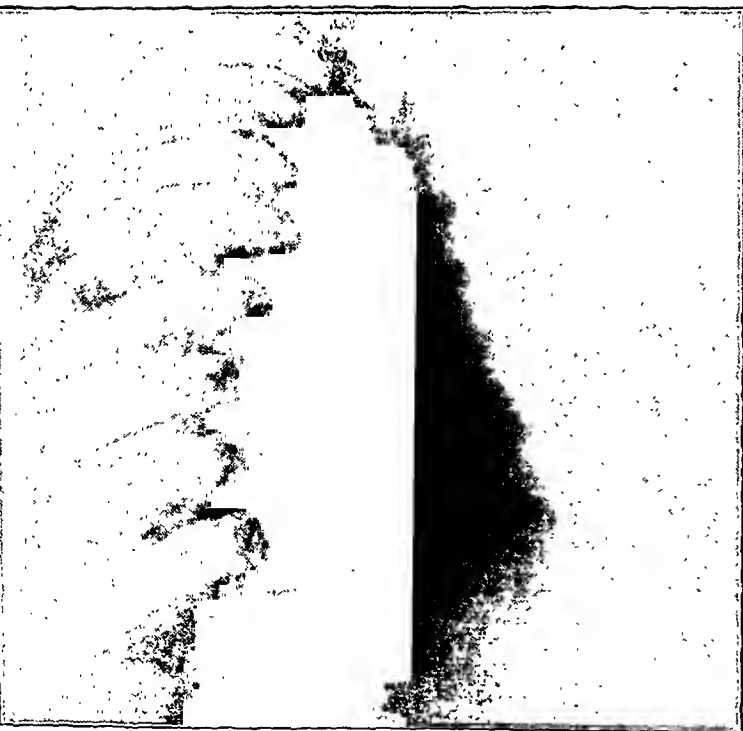


Fig. 2. Case 1.



Fig. 3. Case 1.

PLATE XIX

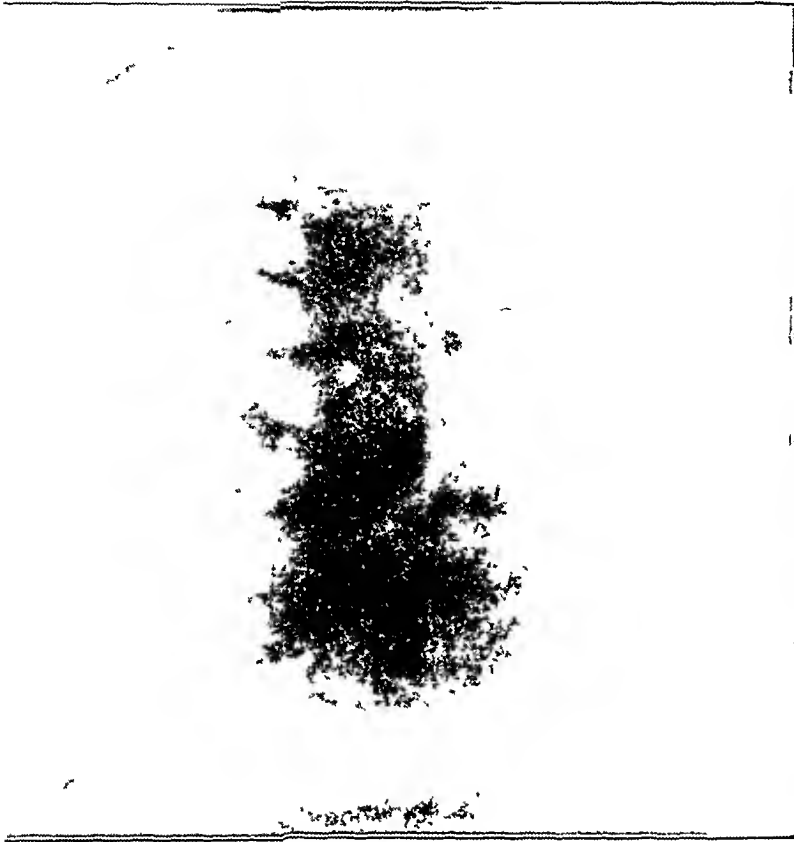


Fig. 4. Case 2



Fig. 5. Case 2



Fig. 6. Case 3.



Fig. 7. Case 3

material containing ascaris ova. This leads us to wonder whether the condition described by us might be a chronic condition caused by the repeated passage of hookworm or ascaris larvæ through the lungs. But if this were so, the eosinophilic condition, being generally believed to be an acute reaction of allergic type, should disappear even if the chronic lung changes remained. We have also observed patients over periods of several months when it was most unlikely that re-infection of any size either with hookworms or with ascaris could take place and x-ray and eosinophilia remained unchanged.

Apart from the question of lesions in the lungs being caused by direct passage of helminth larvæ through them, these intestinal infections are thought by Acton and Dharmendra (1933) and Dharmendra and Napier (1935) to be responsible for a number of cases of bronchial asthma. In the total number of our high eosinophile series there is a high infection with hookworms and other parasites, and a moderate number with *Entamoeba histolytica* and *Giardia intestinalis*, but in the patients who show the 'eosinophile lung' picture, the intestinal infection is less, namely 48.2 per cent, against 64.6 per cent for the whole group, or 71 per cent for the whole group less the selected group of 175. In the highest eosinophile group the intestinal infection is even less than in groups with lower (but still high) eosinophile counts. It seems most unlikely, therefore, that intestinal infection can be the sole explanation.

As regards asthma, the majority of the patients in our series have had cough and other chest symptoms over a long period, but only a few, namely 35, have reported symptoms of asthma or bronchitis, and in only a few of these have we observed typical attacks of bronchial asthma. In any case we can say that typical asthma is not characteristic of this disease.

In conclusion, it may be said that much in this clinical entity points to allergic origin, chiefly because the eosinophilia dominates the syndrome described. But it is possible that there may not be a single agent which causes such a condition, but several.

#### Summary and conclusions

Out of a series of 600 patients with 20 per cent of eosinophiles or more, 175 were found to show an x-ray picture characterized by an evenly distributed extensive mottling of small nodular shadows over both lung fields, with increased linear markings.

Of the 175 patients, 106 had more than 5,000 eosinophiles per c.mm. on admission; 48 per cent had intestinal infection with helminths, *E. histolytica*, or *Giardia*; 69 per cent were tuberculin-negative. The significance of these figures is discussed, and they are compared with the findings for the whole group of 600 patients.

The lung condition found cannot be explained as due to tuberculosis, syphilis or heart disease.

(Continued at foot of next column)

## A NOTE ON TUBERCULOSIS SURVEYS

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CONSIDERABLE interest has recently been evinced by tuberculosis workers in tuberculosis surveys. As to the objects and scope of these surveys, however, there appears to be no clear understanding and the notions about the subject seem to be rather vague. Whilst some are satisfied with carrying out tuberculosis tests amongst a group of school children, others consider a survey incomplete without the determination of the so-called causative factors. In many instances little thought is given to a clear definition of the objects of the survey. They are merely taken for granted and it is believed that the purposes of the survey, whatever they may be, will be amply served by collecting from the patients attending tuberculosis clinics a large mass of information, the larger the better. It will be obvious to anyone who has considered the matter carefully that such an outlook can lead to no results.

Speaking generally, a survey, be it that of a piece of territory or of a section of a community, may be conducted with two objects in view, namely: (1) exploratory or (2) with a set purpose of acquisition of the knowledge of the relevant conditions existing at the time, or likely to develop in the near future, which might help and guide the planning and execution of some proposed constructive work or the putting into effect of some desirable improvements.

(Continued from previous column)

The possibility of its being caused by dust inhalation is considered. The condition is different from Löffler's syndrome. It has some similarity to certain types of bronchial asthma found in India and thought to be connected with intestinal infection. The condition is believed to be allergic in origin.

The importance of blood differential counts in the diagnosis of doubtful cases of tuberculosis is evident.

#### Acknowledgment

We wish to acknowledge the help of Dr. P. V. Benjamin, the present Medical Superintendent, who has been associated with us in this work.

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Very often there is a temptation to wander away from the set object and this must be resisted. Thus if the survey is to serve a useful purpose its objects and scope must be clearly defined, and in the planning and execution these must be constantly borne in mind.

A tuberculosis survey may be conducted with the objects of : (1) Estimation of the extent of the tuberculosis problem in a community, or (2) Determination of what may be conveniently called, the 'herd structure' in regard to tuberculosis. Herd structure in a wide sense would include the state of the community with regard to the extent and nature of sources of infection, the type of the prevalent organisms, the immunity status, and the accessory factors, including climatological, socio-economic and others, favouring or otherwise the spread of infection and disease from the sources to new victims. Besides, one must determine the forces inducing changes in these factors as well as the rates of change. Among these will be included the community effort, both official and non-official, which might be or could be directed towards an anti-tuberculosis campaign.

A third object which a survey might serve is to provide data for purposes of comparison before and after the institution of certain measures relating to prevention or treatment or both. Besides, an investigation into a particular problem, *e.g.*, the effect of a certain industry on the incidence of tuberculosis, may be considered as a special type of survey because the general principles and methods applicable to such an investigation are the same as those of the surveys.

The exact scope of a particular survey will be determined mostly by three factors, namely :—

1. The object,
2. The means available, and
3. The amount of co-operation that can be enlisted, etc.

The question of the objects and scope of tuberculosis surveys has been more specifically discussed in the Report of the Tuberculosis Survey Committee of the Indian Research Fund Association in 1937 to which reference might be made. The committee has envisaged five different types of surveys according to the object in view and have commented upon the circumstances under which they might be carried out and the organization and funds required in each case.

The few tuberculosis surveys which have so far been carried out in this country have been sponsored by clinicians who have specialized in tuberculosis with the result that undue emphasis has been placed on the patient, his diagnosis and treatment, rather than on the communal aspect of the problem. The data have been mostly collected in the dispensaries rather than in the homes of patients. The danger inherent in such a procedure is that the impressions, or even facts, collected regarding those attending

the clinics may be projected to the whole population. Even when precaution is taken to steer clear of this error, it has in most instances been found difficult to draw useful conclusions from the available data, with regard to the population under consideration. It is, therefore, desirable that the survey should be planned properly so that after the data are collected they may be capable of proper analysis and be sufficient in quantity and quality to provide satisfactory information on the main questions. In respect of many items, information will be required for both tuberculous and non-tuberculous families and individuals for purposes of comparison.

To meet these two requirements it is necessary clearly and exactly to set out the nature of the information which will be collected, how it will be classified and how it will be analysed for purposes of instituting comparisons and contrasts, and how the whole scheme will be organized. Proper planning requires considerable critical ability, judgment, experience and expert knowledge of the subject, and it is here that mistakes are often made. Mistakes committed at this stage cannot be corrected later on, with the result that much valuable data go to waste on account of facts vaguely recorded or for lack of information on vital matters, the inferences that can be justifiably made from the available data remain inconclusive. On the other hand, one of the most common failings is to overburden the schedule with a great many unnecessary items which are only vaguely and very indirectly concerned with the points under consideration. Such extra items of information not only cause unnecessary waste of time of the investigators but complicate matters and confuse the issues. No definite rules can be laid down as to how the items of information should be selected or how they should be classified. But speaking generally the following considerations should be kept in mind in drawing up a schedule :—

(1) Each person should bear a serial number, which should in no circumstances be duplicated to designate another individual, nor should one person bear more than one serial number. This rule applies equally to other units of observation such as a village, a house, or a family.

(2) Sufficient information should be included to identify the person who made the inquiry and the date when such inquiry was made. This is necessary for reference. It will facilitate checking and will be found essential in case a correction has to be made.

(3) Necessary information for identifying the individual to whom the particulars in the schedule relate should be included.

(4) Personal information relating to age, sex, etc., should be recorded, so as to work out the usual distributions of population in relation to various problems.

(5) The results of any tests which it is intended to carry out should be noted on standard forms, so that they are comparable.

(6) What other items are included will depend upon the decision as to what hypotheses are to be tested. For this reason definite hypotheses bearing on the problem must be formulated. Thus, for instance, the hypothesis that urban residence tends to immunize the population, and thus modify the course and nature of the disease, may be a matter for investigation. For this purpose it will be necessary to have for comparison groups of individuals who have been subjected to varying degrees of city life ranging from *nil* to complete. The types of lesion in the two groups will then be compared. However, since it is known or suspected that the type of lesion is subject to variation owing to factors other than the one under investigation (e.g., primary or secondary infection, quantum of infection, age, etc.), it is obviously necessary to remove the effects of these disturbing factors or, in other words, to restrict comparison to such groups of urban and non-urban people as are the same in all other material respects. Thus it will be necessary to have a knowledge of the operation of these other factors on each individual under study. This is by no means an easy matter. In many instances either this important point is altogether missed, or, on account of lack of technical knowledge of the subject or methods, it is not properly accomplished. Nevertheless, it is a necessary condition for making valid comparison.

(7) The basis of classification may also present considerable difficulties. Care should be taken to define precisely each class and the basis of classification should be related to the tuberculosis problem. Moreover, the classes should be readily determinable with the means provided. The class intervals should be reasonable in number, neither too many so as to become difficult of defining, nor too few so as to lose significance. A key of instructions should be provided to ensure uniformity of records and intelligent co-operation.

(8) In designing the schedules attention should be paid to the size of paper, print, etc., so that they can be easily manipulated. The same applies to the arrangement of items so that interrogation or recording of observations proceeds in a logical order. Much time and trouble can be saved by appropriately numbering the items of information and the various classes according to the method of sorting which it is intended to apply.

For the convenience of workers and for purposes of securing uniformity, some authoritative body such as the Tuberculosis Survey Committee might prepare schedules for two types of surveys. Those who wish to carry out other types of survey may find the above points helpful in preparing the schedules, and the keys to the schedules. In the absence of previous experience they will probably do well to enlist the collaboration of an experienced epidemiologist in planning the inquiry.

A matter of considerable importance to which only a passing reference has so far been made requires further consideration. While we actually investigate units of population such as individuals, families, houses, or villages our real interest lies beyond them. We are not so much concerned with the particular members or units which are subjected to examination, but our aim is to outline the picture of the community or population of an area in relation to the tuberculosis problem. We wish to see the woods rather than the trees. We should bear this in mind when we proceed to examine the constituents of the community or group for which the picture is required.

It would appear that the most satisfactory picture will be obtained if every member constituting the community is subjected to investigation. This is impracticable when, as is invariably the case, the community is large or many particulars about each individual are to be investigated. Besides for most purposes the desired information can be obtained by examining a sample of the population provided the sample is properly taken. A constituent member of a sample is not there in his personal capacity but in his capacity as a representative of a certain group. Hence care has to be exercised that (a) the various groups or classes of the population, made in reference to the characteristic studied or having a bearing on it, are all represented in the sample, (b) that the relative number of the individuals representing various group are included in the sample in the proportion in which they are met with in the community as a whole, and (c) that the representatives from each group are drawn in a random manner so that there is no conscious selection. Any bias introduced in the selection of representative numbers of a group will vitiate the results on account of intra-group variation. This source of error is not always apparent and must be carefully guarded against. In order that the sample satisfies these criteria it is necessary to know into what classes the population is divisible in relation to the problem under investigation and what is the approximate strength of each class. To settle this point a preliminary survey of the whole community is required. When preliminary data have been collected a good sample may be selected by a man possessing the necessary technical knowledge and experience. Naturally, the more homogeneous a population is, the smaller will be the number of classes, and hence a smaller number of representatives will constitute a good sample. Similarly the intra-group homogeneity will determine the size of the contingent required to represent it adequately. A general rule, to satisfy adequacy of size, can be applied in suitable cases. A sample will be of adequate size if its mean in respect of the characteristics under investigation does not significantly differ from the mean of the population from which it

has been drawn. The deviation of the sample mean from the mean of the population varies inversely as the square root of the size of the sample. In practice this rule does not help because the mean of the population is not known. All that is possible is to take samples of increasing sizes, till a sample size is reached when any further addition will not significantly reduce the difference between the means.

Having secured a representative and adequate sample of the population, the procedure of survey becomes one of technical and administrative organization. The activities of the survey staff may, for convenience, be divided into the following classes:—

1. Securing public co-operation by educating public opinion.

2. Application and interpretation of tuberculin test, clinical laboratory and x-rays examinations of persons suspected of the disease and their treatment. The circumstances under which the open cases are placed with regard to chances of conveying infection to susceptibles should be noted and the results communicated to health authorities.

3. Routine collection, analysis and interpretation of epidemiological and clinical data.

4. Presenting the report.

The success or otherwise of the survey will largely depend upon the administrative and technical capabilities and energy of the officer in direct charge of the survey and the assistance and co-operation obtained from the staff and the public. The money spent upon the survey will be largely wasted if the services of a properly trained officer and other personnel cannot be secured. It is a mistake to assume that a successful clinician with experience of tuberculosis work in a clinic or a hospital will, without epidemiological training and experience, be able to handle a survey efficiently. Unfortunately this mistake has been committed in more than one instance with disastrous results. Apart from other considerations, therefore, it is a sound policy not to undertake complicated surveys, such for example as those designed to elucidate causal factors, unless properly trained and experienced personnel is available.

To obtain the maximum results in the minimum period it is necessary to prescribe the duties and responsibilities of the various members of the staff and the amount of work which on an average is expected of them. The officer in direct charge of the inquiry is the proper person to undertake this task with the consultation of a more experienced worker if necessary. While local circumstances and capabilities of the junior personnel will largely determine the exact distribution of duties, it is necessary to point out that the tendency to devote too much time to the clinic and the office work rather than to the patient's houses must be strongly resisted. The place of work of the surveyors is essentially in the homes and work places. The clinic is

only an auxiliary organization put up for purposes of studying the type of disease in suspected cases. It also subserves a minor function in enlisting the co-operation of public by offering free treatment facilities. Undue emphasis on the clinic work, to the extent of even making it a treatment centre for all diseases, on the plea that thereby public co-operation is secured, has wrecked some survey schemes. It is, for instance, within the knowledge of the author that in a particular survey, in which the officer in charge spent the greater part of his time in the clinic, the perfunctory nature of the home visits was demonstrated by the fact that many a patient in the third stage of the disease was recorded for the first time at the clinic even though the house had been visited a few days previously. It is obvious that in such circumstances little reliance could be placed on the results of home visits. The argument is sometimes advanced that, in the initial stages of the inquiry, contact with the public can be best made through the clinic and later on the routine can be changed to increase home visits. This is a mistaken policy. It may be true that the contact is made more easily through the clinic but it is not the proper kind of contact. It is a wrong approach and as such it does not lead to the right type of public co-operation. Once the public has been taught to expect free treatment, it naturally becomes a demand, and when this is denied or restricted, it stiffens rather than softens resistance. Besides it becomes unintelligible to the lay public why the investigators should interfere with them and undertake the examination of their person and homes when they either have no need for it or do not desire consultation. In drawing up the time-table of the various members of the staff, therefore, the clinic should appropriate the minimum time required for essential service.

In enlisting public co-operation the key position is held by the lady health visitor. It is she that prepares the way for the doctor. Given good personality, tact and a certain amount of leisure she can secure the wholehearted co-operation of the housewife. The visit breaks the monotony of her domestic life and conjures up new hopes of betterment of the family. A man is as a rule more argumentative. He believes that the sacred responsibility of preventing outsiders from crossing the doorstep rests heavily on him and he looks upon any outside intrusion with suspicion. He thinks of all kinds of improbable implications which might adversely affect the welfare of the family. With an ignorant man it is only the outside pressure, be it official or that of public opinion, that breaks the resistance. This method of approach is not very desirable. When, however, the previous consent of the housewife has been obtained he resigns himself to the view that after all it is a domestic affair in which his interference is not really needed. The doctor's visit is now awaited with eagerness, and once



his initial coolness is got over by a tactful remark on the part of the doctor, he is converted into an enthusiast. The confidence in the survey party displayed by the parents is infectious. The children see a lot of fun in their work and they not only willingly submit to the prick of the needle but also wish to participate actively in it by offering their services for odd jobs. The lady health visitor becomes a friend and is followed by a crowd of children from house to house.

With this method of approach the services offered by the clinic are gratefully accepted and not claimed as a matter of right.

To obtain information of maximum value and correctly to appreciate the position in the community is both science and art. The uninitiated will do well to consult an experienced worker, preferably the one who helped him in planning the survey.

These general remarks are offered in the hope that workers undertaking surveys for the first time may avoid some of the pitfalls into which the writer has seen people falling. Details of the procedure for carrying out the survey work have been purposely avoided. For these the report of the survey committee should be consulted. A suggestion which may be finally made is that it will be more profitable if the surveys are systematically made according to a plan rather than in a haphazard manner. If for instance it is desired to frame one anti-tuberculosis policy for the whole province and for that purpose a comprehensive knowledge of the position is required, it will be desirable to select the areas to be surveyed according to the principles of sampling mentioned above. Relatively large samples should be taken for preliminary surveys whose object would be to ascertain the extent and intensity of tuberculosis reaction in various groups of the population and also the incidence of obvious cases, especially those most unfavourably placed as regards treatment and transmission of disease. This type of survey should be followed to determine the morbidity and mortality rates, as well as the type of disease. For this more detailed type of survey smaller units may be selected, particularly from those sections of the community to which the preliminary survey had drawn attention on account of high incidence, or for other reasons.

Surveys for ascertaining the causal factors have been conducted by certain workers in foreign countries. Of these the Tyneside inquiry conducted by Bradbury (1933) is a good sample. It should, however, be realized that such inquiries, if they are to be made properly, require a considerable amount of time and money. Besides, unless a properly trained staff is available these undertakings are not likely to yield results commensurate with the time and money spent on them. Another point which should be taken into consideration is whether the available resources would provide

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## MODERN MEASURES IN THE MASS CONTROL OF TUBERCULOSIS IN THE UNITED STATES OF AMERICA

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### Introduction

RECENTLY I had an opportunity, as the holder of a Fellowship from the International Health Division of the Rockefeller Foundation of New York, of spending a year in the United States of America studying tuberculosis, and I visited most of the important centres and institutions where anti-tuberculosis work is being carried on. A few of the institutions visited by me were: Henry Phipps Institute for the study, treatment and prevention of tuberculosis, Philadelphia; Saranac Laboratory for the study of tuberculosis and Trudeau Sanatorium, Saranac Lake; Bellevue and New York Hospitals, New York City; Herman-Kiefer Hospital, Detroit; Tuberculosis Department of the University Hospital, Ann Arbor; Pottenger Sanatorium, California; Fairview Sanatorium for the Negroes, Michigan; Sanatoria for American Indians at

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sufficient funds for instituting collective measures according to the indications obtained by the survey. Thus, for instance, if it is found that overcrowding is the principal factor operating in the spread of tuberculosis, in a certain area, would it be possible to rectify this defect with the funds that could be made available? It may also be argued that in case funds could be made available for such a desirable object, it is not necessary to await the verdict of a tuberculosis survey to proceed with a scheme of removing over-crowding. However, it must be remembered that the results of a properly conducted survey may provide a convincing argument for educating public opinion and strengthen the hands of the health authority to overcome the inertia and hesitancy on the part of those that hold the purse. In any case, if such a survey is to be made the greatest possible care should be exercised in selecting the area. Unfortunately, statistical data which might guide and help in the selection of the area are practically non-existent in this country. Under the circumstances it is highly desirable not to undertake the survey of causal factors unless the tuberculin survey and survey of morbidity and mortality have been carried out and their results are known. Besides providing the necessary information required for the more detailed survey the preliminary surveys will help in training the personnel and in creating public support.

### REFERENCE

Bradbury, F. C. S. (1933). *Causal Factors in Tuberculosis*. National Association for the Prevention of Tuberculosis, London.

Phoenix, Tucson and Winslow in Arizona; Tuberculosis Divisions of the Departments of Health of Alabama, Tennessee, New York, Arizona and Michigan States and Los Angeles, Detroit and New York Cities.

Besides gaining clinical experience, my studies were arranged in such a manner as to enable me to gain first-hand knowledge of the methods of mass control of tuberculosis which is the subject of this article.

#### *Evolution of modern concepts of tuberculosis control*

Soon after the discovery of the tubercle bacillus the view gained ground that adult tuberculosis was endogenous, that is, the lodgement of the infecting agent took place during childhood and manifested itself in later life on account of certain vague reasons such as the strains and stresses of life which might break open the old, not quite healed, foci, and liberate tubercle bacilli. While it was admitted that in an adult with a positive tuberculin reaction, indicating childhood infection, a massive dose of infection might break down the acquired immunity, it was believed that ordinarily he had no further danger of contracting a fresh infection from outside sources. A little infection during childhood was supposed to protect against a big infection during later life.

For these reasons the anti-tuberculosis campaign was directed mainly along two channels:—

- (a) against the vaguely understood strains and stresses of adult life to guard against the flare-up of dormant childhood infection.
- (b) to protect children in the nebulous hope that they would acquire just enough tuberculosis as would protect them against future infection and no more.

Hardly fifteen years ago these were the prevailing views. The element of direct infection of the adult was either not clearly understood or just ignored.

At this stage two extraordinary developments were taking place in the United States that were destined later to form the basis for the modern, also known as the newer, methods of tuberculosis control.

Ghon and others had drawn attention to the 'primary complex'. First infection or childhood type of tuberculosis, and superinfection or adult type of tuberculosis were studied and understood more and more clearly. Opie (1924) and Opie and McPhedran (1926) of the Henry Phipps Institute of Philadelphia in their pioneer investigations on latent tuberculosis of the lungs brought out clearly that adult lesions represented new infections from without. Simultaneous and subsequent studies by McPhedran, Chadwick, Rathbom (Myers, 1930) and others confirmed these views. With more general use of the x-rays it became a common experience to find apparently perfectly healthy people with grave

progressive lesions of the lungs. The pathology of onset of tuberculosis was understood in a much better fashion. All this helped to bring the contagious nature of tuberculosis into prominence.

The other development of far-reaching consequence was a country-wide programme to wipe out tuberculosis in cattle by slaughtering every animal that showed evidence of infection. In the beginning it met with great opposition on the part of cattle owners because it involved the destruction of a large number of cattle and sometimes of whole herds. Some compensation was paid for the animals killed but it fell far short of their actual value. Later, however, with better understanding of the owners that it was being done for the protection of the rest of their cattle, the campaign proved a complete success. Within a few years the infection among cattle was reduced to a minimal point. In many areas the rate of tuberculous cattle is less than 0.5 per cent to-day (*J. A. M. A.*, 1934). This achievement has proved an eye-opener to physicians. What can be accomplished in bovine tuberculosis can also be achieved in human tuberculosis. Of course the drastic method of sending every tuberculin-positive animal off to the slaughter house cannot be applied to human beings but there are other means of achieving the desired end. Human beings with tuberculosis can also be prevented from infecting healthy people, and this can be brought about by intelligent management of patients either in their homes or in an institution until they improve to a stage when they are no longer dangerous for others, or failing that, until they die.

Thus, the discovery of exogenous infection of adults supplemented by the dramatic results of the direct attack on bovine tuberculosis in the United States gave shape to the modern campaign against tuberculosis which, to quote Long (1935), 'centres around the patient with open tuberculosis expectorating bacilli. Reduced to its simplest terms the object must be to find the open case, and bar it as a source of contagion to others'.

It is generally admitted that environmental factors and resistance-lowering influences such as poverty, over-crowding, poor housing, malnutrition, inadequate medical care and lack of education play a considerable part in the drama of tuberculosis, but these are considered as contributory causes facilitating the spread of infection. The prime object of a modern campaign is to find the spreaders of infection, and once they are found, to keep them from being the source of contagion to others.

#### **TUBERCULOSIS CONTROL MEASURES**

The modern programme of tuberculosis control in the United States can be divided into two broad categories, case-finding and case-supervision. Every effort is made to maintain a proper and constant correlation between the

two. This is facilitated by having a unified direction of effort towards case-finding and case-supervision. So far as governmental agency goes, the entire programme, right from the organization of hospitals down to the education of the public at large, which is a necessary adjunct to a successful case-finding programme, is the concern of one department only, the Department of Health. In the various States the responsibility for the programme is usually placed in the Division of Tuberculosis of the State Department of Health. A Director of Tuberculosis responsible to the State Commission of Health is in charge of this division.

In view of the communicability of the disease the following procedures are considered essential in the administration of control measures :—

- (i) Reporting and registration of cases of tuberculosis.
- (ii) Active and progressive case-finding.
- (iii) Provision of modern hospital care and treatment for tuberculosis cases.
- (iv) Domiciliary supervision of families in which tuberculosis is or has been a problem.
- (v) Follow up of all cases and contacts.
- (vi) Rehabilitation of cases.
- (vii) Financial assistance to needy families.
- (viii) An educational programme for the medical and nursing professions and public through institutes, demonstrations, lectures, exhibits, motion pictures and literature.

In addition to the above-mentioned programme, the department of health carries out periodic appraisal and evaluation of procedures and services from the point of view of administrative economy and of expansion of our knowledge of the epidemiology and pathogenesis of the disease. It regulates, stimulates and assists research work.

It is impossible in this brief article to describe in detail the various procedures just mentioned. An attempt may however be made to mention a few important factors. It may be noted that in the different states the procedures may vary in some detail according to the conditions prevailing there, but the fundamental problems are the same for all communities.

#### *Case-finding*

It is of prime importance in any communicable disease that the sources of infection be found.

Since tuberculosis in cattle has been so well controlled in the United States there remains only one important source of tubercle bacilli and that is the person who has tuberculosis. Forms of tuberculosis other than pulmonary are comparatively rare and therefore are not so important as sources of infection, but occasionally they also can disperse bacilli and are not altogether ignored.

It is important to find persons who have tuberculosis before they have become 'open'

eases because, at this stage, not only can they be treated with far greater chances of recovery, but also they cannot have done any harm to others. However, it is common experience in the United States even to-day to find 80 per cent of cases reported to be in the moderately and far advanced stages of the disease.

Tuberculosis is such an insidious disease that a person suffering from it does not generally seek advice until it is well advanced. It is therefore of great importance in the successful conduct of the control programme to go out into the field and find him. This is the primary function of the tuberculosis clinic. The clinics are usually permanent, and the tendency to-day is to have them either as a part of a tuberculosis hospital or to run them under close supervision of one.

Formerly, tuberculosis clinics, and for that matter all tuberculosis institutions, were largely organized by private philanthropic bodies such as the National Tuberculosis Association and Charities Aid Association of New York State. Their policy was to demonstrate to the government as well as to the people the practical methods of tuberculosis control. The great value of the institutions was soon recognized and state, county and municipal sanatoria and clinics followed so that to-day most of these institutions are state-controlled.

The ideal in view now is to expand the network of clinics and sanatoria and to cheapen the methods of diagnosis to such an extent that the entire population has a periodic health examination sufficiently complete to rule out tuberculosis, but as yet this is not practicable. It is practicable, however, to find out special groups in the population where tuberculosis is more prevalent than others and to concentrate our efforts on them. Examples of such groups are contacts of open cases, men in hazardous occupations like those exposed to silica dust, inhabitants of congested areas and adults.

In the recent past, school surveys have been very popular. School children form a group that can be easily regimented, and some believe that such surveys have great educational value. Moreover, anything done for the children appeals to the public fancy. But now, through experience, it has been realized that for case-finding it is not a fruitful procedure. Children of school age have very little clinical tuberculosis and almost never have it in a communicable state. If these children are really to be protected we should direct our efforts towards older groups where the spreaders of infection are to be found.

This has been most strikingly brought out by Plunkett in reporting the experience of New York State Tuberculosis Clinics. He states (quoted by Douglas, 1939) that because of the large number of persons that must be examined to find a case, it costs over 4,000 dollars a case to find tuberculosis in the age group from 0 to 14, whereas from 15 to 24 it costs only 187

dollars and grows less with each decade until after 45 years it only costs 77 dollars per case.

Thus, from the point of view of case-finding it is far more profitable to concentrate on college populations and older age groups than on school children. The educational value of such surveys among school children is also doubtful.

School surveys, however, have one value. When the number of tuberculin positives is low in a community, say up to 40 per cent, then the infection in a child may imply contact at home and it may help in tracing the source cases, in many instances. In the United States the infection rate is usually much higher than 40 per cent.

In communities where the reactor-rate among adults is relatively low the best way to carry out such surveys is to make a tuberculin test of all members of the group and to x-ray the positive reactors. Where the tuberculin reactor-rate is high there cannot be much saving in tuberculin-testing before resorting to the more expensive x-ray examination of the chest.

Great efforts are being made to lessen the cost of x-ray examination. Some of the methods that have been devised are mentioned below :—

(a) Fluoroscopy is coming into prominence day by day. Fluoroscopic examination of the lungs is not commonly believed to be as valuable as examination by x-ray films, but as an aid to further selection of the persons before x-raying them it has come to acquire a place in the routine procedures of several well-known institutions in the United States. The lesions suspected with the fluoroscope are always confirmed in roentgenographic films.

The advantages of fluoroscopy over x-ray films are that it is less expensive and more expeditious. The drawbacks are that this method requires trained medical personnel to make the examination and there is no permanent record other than the description dictated by the observer.

Experimenting on a large series of cases, the Metropolitan Life Insurance Company of New York has adjusted the relative values of the various methods of case-finding as follows :—

X-ray	..	100 per cent (arbitrary)
Fluoroscopy	..	87 per cent
Physical examination	..	36 per cent
History	..	33 per cent

(b) Paper films have been used extensively in mass surveys as a screen and suspected cases are x-rayed on celluloid films. Recently paper films in use in New York clinics have been greatly improved and in the opinion of some workers they are proving as good as celluloid films.

(c) Photographing the fluoroscopic image on 35 mm. film, sometimes called 'micro films', has been tried in several places, but on account of the tremendous magnification to which the film must be subjected for the reading of results and

consequent considerable loss of detail, this is not generally considered satisfactory.

(d) At the Herman-Keifer Hospital in Detroit, Michigan, Drs. Hollis Potter and Bruce H. Douglas, in collaboration with the General Electric X-ray Corporation, are developing a method of photographing the fluoroscopic image on a 4 × 5 x-ray film that holds promise of providing an economical and yet satisfactory film that will obviate the necessity of magnification for routine examination. I had the privilege of reading a number of these films with Dr. Douglas and after some practice found no difficulty in making out even very small lesions without magnifying the film.

### *Isolation and treatment*

Having found the cases the next logical step is to isolate and treat them.

In early days sanatoria were as a rule situated far away on mountain tops or in deserts. The functions of a sanatorium in the United States were at best those of a first-class boarding house under medical supervision, where advanced and moderately advanced cases lived for a few years of comparative comfort.

An epochal step was the inauguration in 1908 of the International Congress on Tuberculosis in Washington, D.C., which was attended by outstanding leaders from all parts of the world. The proceedings of this convention gave precision to the existing knowledge of the disease and the principal recommendation made was that 'institutional treatment of tuberculous be given as a preventive measure'. This fact, together with the development of the idea to 'cure the patient in the climate in which he expects to live', brought the sanatorium close to the door of the people. More recently, with better knowledge of the epidemiology of the disease and improved methods of treatment, a modern sanatorium (the term hospital is preferred) is the virtual headquarters for all anti-tuberculosis work in the area it serves. Besides treatment of the patients such an institution runs a diagnostic out-patient service, guides and assists local authorities in conducting case-finding clinics, provides medical and technical experts for examination and portable x-ray machines where needed, helps private practitioners in the diagnosis and treatment of tuberculosis, supervises public health nursing services, initiates and helps surveys of students and other special groups, trains public health nurses and social workers for tuberculosis work, provides instruction to medical students and pupil nurses and post-graduate instruction to physicians and, finally, serves as a centre for tuberculosis research.

It is a hospital of this type that Plunkett (1938) has in mind when he says that 'The modern tuberculosis hospital and the well-equipped, well-conducted case-finding and follow-up clinic are society's most valuable administrative weapons against this disease.'

They are more formidable still when combined into one service'.

Years ago, a careful socio-medical study of tuberculosis in a representative community was conducted in Framingham, Massachusetts. On the basis of this study a minimum standard of one bed for each annual tuberculosis death was arrived at. More recently, Chadwick (1933) has recommended a goal of two beds per death and this is now generally recognized as representing the minimum requirements of a community for adequate hospitalization of the tuberculous.

The annual average number of tuberculosis deaths in the United States is 70,000. There are about 1,300 institutions containing 100,000 beds, or a ratio of 1.4 beds per annual death. The aim is to have at least 50,000 more beds so that the standard of two beds per death is achieved.

For large cities the goal of two beds per death is within the range of possibility of attainment and in the long run they save money by providing the required facilities, thus eliminating a terrific economic drain in loss of life and man power. For the rural areas and small towns, however, it seems difficult, if not impossible, to achieve even the minimum standard, particularly because a vast majority of these patients can pay little or nothing towards the cost of their treatment. In this connection a quotation from the Report of the Committee on 'Tuberculosis Among Negroes (1937)' published by the National Tuberculosis Association is illuminating:—

'The important rôle which sanatorium treatment plays in any programme for the control of tuberculosis is almost universally recognized. We wish to emphasize, however, one fact which is sometimes overlooked, namely, that adequate facilities for hospitalization are doubly important in dealing with the Negro tuberculosis problem. The Negro race as a whole, being in the lower economic stratum, lives in greatly over-crowded quarters the presence in which of an open case of tuberculosis often exposes relatively large numbers of individuals to massive and repeated doses of virulent tubercle bacilli. There are rarely facilities for caring for the patient at home, the diet is usually inadequate, and there is in most instances a dearth of knowledge as to what should be done. In the vast majority of Negro homes it is utterly impossible to provide for the patient those things which we know are essential for his recovery and equally impossible to give any adequate protection from infection to other members of the family.'

When it is difficult to provide adequate facilities for the hospitalization of the tuberculous there are certain measures which while less effective are also less costly and it is quite justifiable to promote the use of such temporary measures.

#### *Burr cottages*

In the Southern States poor families in rural areas live in one or two-room shacks. Their families are usually large. An open case in such a family has no chance whatever to rest and it is impossible to protect other members of the family from infection. In such circumstances Burr cottages are being used extensively

in the absence of proper hospital accommodation.

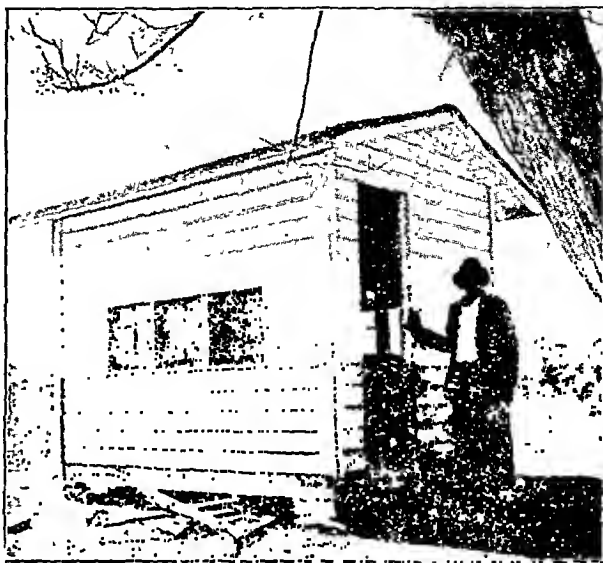


Fig. 1.—A Burr cottage.

The Burr cottage is a wooden structure usually 8 feet  $\times$  10 feet. It is screened and ventilated and can be easily carted about in a truck by unscrewing the six parts—four for the sides and two for the roof and floor. The cottage is fixed at a short distance from the residence of the family and, where climate permits, a patient can remain in the cottage throughout the year. With the help of an adequate public-health nursing service and a capable physician a great amount of benefit can be derived both by the patient and his associates.

#### *Screened porches*

Many homes in rural areas have porches which if screened can serve as fairly satisfactory quarters for a tuberculosis patient.

#### *Homes for custodial care*

These are 'homes for incurables' which furnish custodial care rather than sanatorium

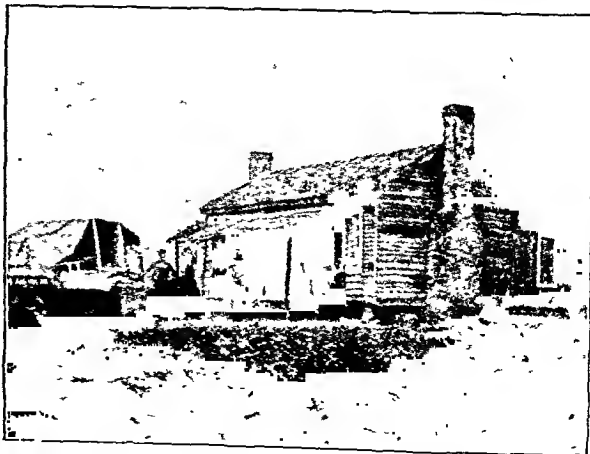


Fig. 2.—A Negro home in the south being screened.



treatment for far-advanced cases and are found chiefly in Southern States for the benefit of the negro community for whom facilities for hospitalization are far short of requirements. These provide the patients with essential medical and nursing care, adequate food and a place to rest at a comparatively low cost and at the same time take out of circulation open cases of tuberculosis.

#### *Ambulatory pneumothorax clinics*

In Philadelphia and Chicago, ambulatory pneumothorax clinics have been developed with considerable success. Selected cases, such as arrested cases, cases with negative sputum, or those who are waiting for accommodation in a sanatorium, are given ambulatory treatment. This plan, although no substitute for hospital care, provides some treatment for a number of patients who would otherwise go without it and also has value in training physicians. An outstanding example is the large chest clinic of the Henry Phipps Institute, Philadelphia.

#### *Beds for the tuberculous in general hospitals*

During recent years there is a definite trend towards the use of beds in general hospitals for tuberculosis patients. By 1938, one hundred and seventy-seven general hospitals in the United States had made arrangements for the care of tuberculosis patients. An outstanding example is the University Hospital, Ann Arbor, Michigan. Two whole floors of this hospital are reserved for tuberculosis cases. Some Canadian provinces are so convinced of the utility of this plan that all general hospitals receiving governmental aid are required by law to reserve 10 per cent of their beds for this purpose. To be fully effective this arrangement calls for careful supervision by the staff of a close-by sanatorium.

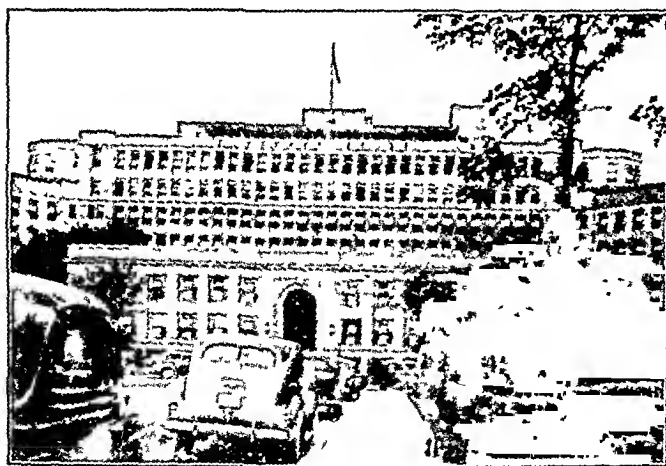


Fig. 3.—University Hospital, Ann Arbor, Mich., where two whole floors are reserved for tuberculosis cases.

#### *Collapse therapy as a public health procedure*

Unfortunately there is no specific for this disease. There is no drug similar to quinine in malaria, no antitoxin as in diphtheria. Indirect methods of treatment must be relied upon.

In the past, reliance was placed on rest in bed, and with less justification, on climate and altitude. On analysis of the reports from institutions in various parts of the United States, some noted for their climate, others not, the results are found to be essentially the same and most disappointing except for minimal cases. For this reason many institutions, until recently, admitted only 'early' cases. Obviously such institutions were not contributing much toward the control of the disease, for the patients with advanced disease who were refused admission were the very cases that were keeping tuberculosis a serious problem in the country. If they could be got out of the way, 'early' cases would not be developing.

Collapse therapy has changed the picture. A large percentage of cases who show no signs of progress on rest in bed alone show rapid improvement on collapse of the tuberculous lung and, what is most important from the public health view-point, the output of tubercle bacilli is cut short. The present view is to employ collapse therapy as an epidemiological procedure rather than as a therapeutic individual measure. Another great advantage gained is that by this means it has become possible for a sanatorium to convert ten or more open cases to closed cases per bed as against 'curing' one or two cases only per bed every year. This is of particular significance in areas where bed accommodation is limited. It is understood that the programme includes an efficient follow-up service and that necessary facilities for refills at proper intervals exist in the locality where the patients reside.

#### *Follow-up and rehabilitation*

A very important part of a tuberculosis programme is the provision of effective medical 'follow-up' to see that improved cases are properly advised and the least signs of reactivation of the disease detected before any harm is done to them or before they become open cases and a menace to others again. Such supervision is exercised either by the local public health department or by the sanatorium service. In

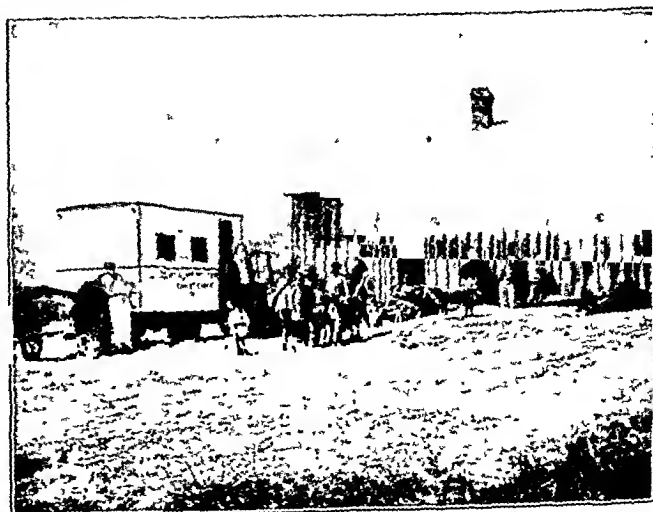


Fig. 4.—Free mobile x-ray facilities for diagnosis and follow-up are available in most States.



the case of the former, on account of their multifarious and apparently more urgent duties, often a very secondary place is relegated to this activity.

Rehabilitation of ex-patients is perhaps the most difficult problem to tackle in the tuberculosis campaign. There are several reasons for it. In the United States, compensation laws make it very difficult for a person with this handicap to be employed in industry. There is a general prejudice in the public mind against the employment of such persons. Then again, of the 100,000 patients who are discharged annually from the 600 odd sanatoria in the United States it has been estimated that about half of them need vocational training to fit them for a productive life.

Rehabilitation is the least developed phase of the anti-tuberculosis programme. The National Tuberculosis Association are making an intensive study of the problem and have launched an experimental programme in various sanatoria throughout the country. Provision of sheltered occupations is finding favour and is being pushed.

#### *Reporting and registration of cases*

Any attempt to control tuberculosis, in the absence of good reporting, will be futile. It is only when we know accurately the incidence of the disease that we can judge how and where to direct our activities to the best advantage. Moreover, in the absence of reliable and complete vital statistics we cannot evaluate the success of our programme. The paramount importance of the practitioner, who is consulted by a large majority of patients in search of diagnosis, is therefore obvious. Much depends on his ability to diagnose early cases and the amount of co-operation he extends in the way of notifying and advising the patients and their associates.

There are several reasons why a physician may fail to report. Among them are indifference or under-developed sense of responsibility towards the public, a desire not to displease the patient who wishes to conceal his disease and unwillingness to permit health department agents to visit the patients. All these objections have to be met and can be met by mutual understanding.

For the physician to be able to diagnose early cases and to administer the most modern forms of treatment special training is necessary. Several means are employed to achieve this and to fit him for anti-tuberculosis work.

(a) *Internships and residencies* in hospitals and sanatoria are the best means of imparting special training to physicians in the diagnosis and treatment of tuberculosis.

(b) *Special courses*.—An outstanding example is the comprehensive course held at Saranac Lake regularly every year. Eminent authorities on various phases of tuberculosis from several institutions participate in this course.

(c) *Teaching clinics*.—These have proved useful in training negro physicians. The first one was organized at Memphis, Tennessee, on a co-operative basis, the clinician in charge being provided by the National Tuberculosis Association, nursing service by the city health department, and clinic space by one of the negro hospitals. Negro physicians are invited to bring their patients personally to the clinic for expert consultation. The clinic is held once a week. The clinician in charge makes a careful examination of the patients, explaining and demonstrating his findings to the attendant physicians. It is, however, made clear to the family physician that the patient is to be under his care whatever the findings. Many other cities have adopted this plan.

(d) *Institutes for physicians*.—A short but very intensive programme of lectures and demonstrations by outside physicians of repute is arranged periodically, the object being to arouse and maintain the interest of physicians in tuberculosis and also to bring to their attention from time to time new developments in the diagnosis and treatment of tuberculosis. These are becoming very popular.

#### ANTI-TUBERCULOSIS LEGISLATION

In New York City, a generation ago, an ordinance was passed making it possible for the authorities to arrest and imprison an incorrigible consumptive, i.e., an open case of tuberculosis who after repeated warnings refused to obey the regulations concerning the destruction of sputum and other measures to prevent his spreading infection among his family and associates. The enforcement of this law was impossible for ethical and social reasons as well as because of the great numbers involved, but there is no doubt that it had a good warning effect on the negligent patient and also helped in drawing the attention of the public pointedly to the danger of an open case. Since then most communities in the United States have framed more practical laws for the control of the disease in the light of its communicable nature.

Anti-tuberculosis legislation falls into two categories, coercive and enabling. Coercive laws are directed towards the prevention of spread of infection by making the reporting of cases by physicians mandatory and by enjoining all such precautions as are necessary to prevent the transmission of the disease from the sick to the well. Enabling laws permit the governmental bodies such as State Boards, Municipalities and County Councils to raise funds to meet the cost of the various procedures of the control programme and to put them into execution.

#### *Conclusion*

The control of tuberculosis in the United States is by no means an accomplished fact, but the tremendous and far-reaching advances in the knowledge of the disease that have taken place during the past decade have brought the

ultimate victory over this age-old foe of mankind within the realm of possibility. There has already been a definite reduction in the death rate from tuberculosis, the rate now being less than one-third that which obtained at the turn of the century. Dr. H. R. Edwards, Director of Tuberculosis, New York City Department of Health, sums up the position in these words: 'If we had no further knowledge than that now available there is no reason why with the proper application of methods the disease cannot be eradicated'.

Finally, I may quote the words of Dr. Esmond R. Long, Director of the Henry Phipps Institute, Philadelphia, from his lecture to the Medical Association of Puerto Rico: 'The way seems perfectly clear. The mechanism for the control of tuberculosis is understood. In the same general form as in the United States, with modifications to suit each local situation, it is proving effective throughout much of the world to-day. Admittedly the cost is great. But the chief requirement is an aroused public interest and it is highly gratifying to see this public interest rising throughout the Americas'. Thanks to the initiative of Her Excellency the Marchioness of Linlithgow the same is coming true of India too.

#### Summary

Before the bacterial origin of the disease was known the public health campaign against tuberculosis lacked specific direction. Emphasis was laid on the unfavourable conditions of life that helped in producing this disease. With the discovery of the tubercle bacillus the communicable nature of the disease was established, but it took almost two decades before this fact was fully appreciated.

More recently extensive studies on the exogenous mode of infection in human beings and the virtual eradication of bovine tuberculosis in the United States have brought the contagious nature of the disease to the fore, and have led to the attention being focussed on the elimination of the opportunity for infection in the mass control of tuberculosis.

The key-note in the modern anti-tuberculosis campaign is to find the open cases of tuberculosis and, having found them, to isolate and treat them. A constant and proper correlation between case-finding and case-supervision is essential for the successful conduct of the programme. This is best achieved by having a unified control over the two activities. A close co-operation between the medical practitioner, philanthropic organizations and the governmental public health department is further necessary for the success of the programme.

In the finding of cases, when the means at our disposal are limited, it is best to concentrate on groups likely to yield the greatest results. Examples of such groups are contacts of open cases, inhabitants of congested areas, workers exposed to silica dust, and adults.

School surveys are not a fruitful means of case-finding, but can help in locating source cases in communities where infection rate is not very high.

Tuberculin-testing all members of a community and x-raying the positive reactors is perhaps the best method to detect cases. X-raying is still a very costly procedure. Alternative methods are being devised to cut down the costs without affecting the efficiency in diagnosis.

The isolation of open cases in a sanatorium is of the utmost importance in the mass control of the disease. A standard of two sanatorium beds per annual death is considered the bare minimum requirement. Where this standard cannot be achieved certain compromise measures are adopted. Treating tuberculosis cases in general hospitals is becoming increasingly popular.

Collapse therapy is now looked upon not only as an individual therapeutic measure, but as a public health procedure of great significance. With its aid, cavities get closed and sputum is rendered negative much sooner than is otherwise possible. This cuts down the spread of infection and also enables the hospital beds to register a quick turn-over of cases.

The after-care of the discharged patient and his rehabilitation into the community are as important as the treatment, but, while the treatment is the best developed and the most successful part of control programme, the follow-up and rehabilitation are the most difficult and least developed phases of the campaign. Vocational training and sheltered occupations seem to hold the best promise for a solution of the perplexing problem of rehabilitation.

Private practitioners constitute the first line of attack. To be able to diagnose early cases and to administer the latest forms of treatment call for their special training. It is still more necessary in the case of physicians who are to run clinics, hospitals and sanatoria which form the most vital part of anti-tuberculosis programme.

Legislation of 'enabling' and 'coercive' types is considered necessary in the United States to empower the governmental bodies to provide necessary facilities and to enforce such measures as aim at preventing the spread of infection.

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# Indian Medical Gazette

OCTOBER

## A TUBERCULOSIS POLICY FOR INDIA

An important part of almost any public health scheme is the education of the public—or propaganda. Propaganda is a wide term; it doesn't simply mean warning the people of the existence of an evil—tuberculosis in this instance—and working them up into a state of panic, nor, on the other hand, telling them that they simply have to do is this or that, and all will be well—with them and their families at least. It is much more comprehensive than this. Unfortunately, during the last few years the word has acquired an unpleasant sound and has almost come to mean the repetition of an untruth so frequently that even those who originated it believe it. Propaganda may take many forms and its objects are manifold, but above all public health propaganda should aim at presenting to the people the truth and the whole truth, in as concise and comprehensible a form as possible.

A story was once told, of an Irishman who had got himself and his companions into so much trouble by his elaborate prevarications that they all agreed that the only way out of their difficulties was to make a clean breast of the whole affair and tell the truth. 'But', said the Irishman, 'we must first decide what the truth is to be!' So it must be with propaganda. We must decide what the truth is to be before we attempt to tell it to the people. That is to say, it is essential that we should first have a clear conception of our policy. We must not start off vigorously in one direction and advocate one particular measure as the only possible one to adopt, then, finding it impracticable, decry it and say 'perhaps after all that wasn't the best measure to adopt' and turn our propaganda machinery in another direction: any such suggestion of vacillation will be fatal. Though it is true that we do not know the whole truth about any medical subject and that research is always bringing to light new facts, we do know a very great deal about tuberculosis, its cause and the way it is spread, the methods by which it can be prevented and its treatment; we also know the extent of its ravages in this country, and the limitation of the public purse for putting into practice these methods of prevention and treatment. We should therefore be in a position to adopt a definite policy, one that is capable of unlimited extension and, without alteration of the main structure, modification, as new facts come to light and new discoveries are made.

It has been emphasized repeatedly by tuberculosis workers in this country that we must not adopt a tuberculosis policy directly from some more advanced country and graft it on to Indian conditions. We must shape our own policy; this policy must be based (a) on the scientific knowledge that has been gathered from the study of tuberculosis throughout the world, (b) on the special knowledge that workers in this country have gathered regarding the deviation of the disease from the universal picture, to which should be added, with caution, observations made in other countries with climates similar to those of India, (c) on our knowledge of the habits and state of education of the peoples of India and of the administrative framework on which the policy will have to be grafted, and finally (d) on a proper estimate of the funds that are available, are likely to be available, or could possibly be made available, *vis-à-vis* the economic state of the country.

In Great Britain the sanatorium is the central point of the tuberculosis policy, but in India it would be absurd to advocate a policy of sanatoria for all, because we know that such a policy could not be financed now, nor in the near future, nor even in the more distant future as far as this concerns us, our children, or even our grandchildren. On the other hand, as sanatorium treatment is the treatment of choice, in this as in any other country, we must not take the reactionary attitude that sanatoria are luxuries India cannot afford, for even if, through necessity, the centre of gravity of the tuberculosis campaign is in the dispensary, or tuberculosis clinic, the sanatorium should be the ideal at which we aim, and any comprehensive scheme must include a large number of sanatoria in different parts of the country, to stand so to speak behind the tuberculosis clinic.

We open this number with a paper by the medical commissioner to the Tuberculosis Association of India on 'organized home treatment'. Realizing that the vast majority of patients cannot hope to receive institutional treatment, and that in the ordinary way 'home treatment' means no treatment at all, Dr. Frimodt-Møller has outlined a scheme for 'organized home treatment'; this is more comprehensive than the title suggests and is in fact a scheme for the control of tuberculosis in India. He has laid down certain measures as being essential if 'home treatment' is to have any real meaning; these are:—

- (a) The tuberculosis clinic, which is to be not only the centre of diagnosis, active treatment, and dispensing, but the spiritual centre of the movement from which should come inspiration and advice to the local practitioners and the lay workers.
- (b) Hospital wards and sanatoria where selected cases are treated, and where accepted forms of treatment are used and their efficacy demonstrated, and

any new and promising forms of treatment are tested. These should be the most important centres for training tuberculosis experts.

- (c) Close co-operation between the local practitioners and the tuberculosis clinic.
- (d) Welfare committees who will co-operate with the clinic and other tuberculosis institutions.
- (e) 'Colonies or settlements for tuberculous ex-patients'.

It is only within such a framework that 'home treatment' can possibly be successful. The necessity for provision of hospital wards specially reserved for tuberculosis and/or sanatoria we have already emphasized, and, in these days of more active and surgical treatment, it is becoming increasingly important that there should be a tuberculosis ward in every large general and teaching hospital, as it is not only the specialist that should receive instructions on this disease, but every medical man and woman in the country.

The clinic, as we have suggested, will have to be the pivotal point of any tuberculosis scheme in this country for many years to come, and the necessity for close co-operation on the part of the local medical practitioner on one side and the welfare workers on the other is obvious. It is only when we come to the place of 'colonies or settlements for ex-patients' that a little doubt arises in our minds and we begin to wonder whether this is perhaps not an attempt to copy too closely western methods.

It is of course possible that this writer has in his mind a kind of convalescent section of a sanatorium, where patients who do not require any active treatment and are fit to do light work should be placed for a number of months or even years. Such a scheme is in all probability practicable but beyond this we doubt if it would be advisable to go in following methods suited to western countries. There, conditions are very different; the majority of the people are urban dwellers, and their work is of such a nature that the individual crippled by tuberculosis is unfit to return to his previous employment; there is seldom any place for a 75-per-cent man in modern industry and if he attempts to hold his own he will inevitably break down, so the colony or settlement had to come into being. But is it the same in India? Undoubtedly, parallel cases could be found, probably hundreds of them, but they are the exception as 90 per cent of India's population live in rural areas and a very large proportion of the urban dwellers keep in close touch with the villages from which they originated and will insist on returning there when their health breaks down or they require a rest. Such people will willingly stay in hospital or in a sanatorium, but it seems doubtful if they could be persuaded either to uproot their families from their traditional surroundings or to cut themselves off from them, even if it

would be economically sound to recommend such a procedure on a large scale. The life of the cultivator in India may not be a very easy one, but the strain that is put on him is not comparable to that to which the average worker in the west has to submit, and some light task by which he can help to earn his daily rice can usually be found for him.

With this possible exception we are in entire agreement with the medical commissioner's minimum requirements and his scheme for organized home treatment. He has outlined a scheme that can be adopted now and is capable of infinite expansion, as funds become available and the education of the public progresses.

L. E. NAPIER.

## THE SPECIAL TUBERCULOSIS NUMBER

For the fifth successive year we are issuing a special tuberculosis number. As in previous years, we have had the assistance and advice of some of the leading tuberculosis workers in India, and this year a special editorial committee of the Tuberculosis Association of India has collected and selected papers and other matter for inclusion in this special number.

The editorial committee consisted of Dr. C. Frimodt-Møller, the medical commissioner of the Tuberculosis Association of India, Dr. A. C. Ukil, one of the pioneer research workers in tuberculosis in India, and Dr. Sikand, until recently secretary of the Tuberculosis Association of India. The editorial committee wish the number to be representative of expert opinion generally in India and not only of their own views, or of those of the officials of the Tuberculosis Association of India; in recommending the papers for publication, the committee do not necessarily identify themselves with the views expressed. The final selection of the papers for inclusion in the number rests, of course, with the editor.

## Medical News

### TUBERCULOSIS ASSOCIATION OF INDIA

#### TUBERCULOSIS NEWS

*Broadcast talks.*—The Tuberculosis Association of India has inaugurated a series of broadcast talks on 'Tuberculosis—A Menace to India' from the Simla Radio Station.

The subject of the first talk delivered by Her Excellency Lady Linlithgow, the President of the Association, on the 5th July was 'Meeting the Menace'. Her Excellency referred to the spread of the disease in India, the steps so far taken to meet the menace and laid stress on the necessity for the training of doctors who could take charge of clinics and other tuberculosis institutions. She closed by stating that with the will to understand the problem, and with the co-operation of the individual in every walk of life, from the big industrialist and employer of labour to the poorest inhabitant of his village, success will be obtained in the campaign against tuberculosis.



Major-General G. G. Jolly, Chairman of the Association, delivered the second talk of the series on the 17th July on 'Organized Fight against the Menace'. He explained the policy advocated by the Association—not as the only policy to be adopted, but as a useful step that could be taken at the present stage of development—respecting the control of tuberculosis by organized home treatment. He emphasized that if the scheme of organized home treatment was to succeed, there were five main activities which must be carried out in association with it. Firstly, establishment of modern tuberculosis clinics; secondly, creation of facilities for institutional treatment of selected patients; thirdly, closest possible co-operation between clinics and private practitioners; fourthly, formation of cure and after-care committees; and, fifthly, establishment of colonies or settlements for tuberculosis ex-patients.

**Research.**—(a) According to a decision of the central committee until such time as the Tuberculosis Association of India is in a position to undertake independent research work in tuberculosis, it should co-operate with the Indian Research Fund Association. With this end in view a sum of Rs. 4,000 has been paid to the Indian Research Fund Association for an epidemiological enquiry on tuberculosis under Dr. R. G. Cochrane, Chief Medical Officer, Lady Willingdon Lepet Settlement, Chingleput, Madras.

(b) A tuberculosis survey is being carried out in Vayalpad by the authorities of the Union Mission Tuberculosis Sanatorium, Arogyavaram, near Madanapalle (Madras). Up to the end of May 1940, they had examined 2,000 persons out of whom more than 45 per cent were found infected with tuberculosis. From these positive cases, strongly reacting cases were taken to the sanatorium for x-ray examination and 48 were detected to be suffering from the disease.

**Provincial Tuberculosis Associations.**—(a) The Bengal Tuberculosis Association publishes a monthly journal in which, apart from news of general interest, articles by distinguished tuberculosis workers are reproduced. The annual subscription is Rs. 3, inclusive of postage.

The Bengal Association has raised so far during the current year a sum of Rs. 14,000 by a charity performance and an appeal for the 'Kalyani X-Ray Fund', the income from the latter being used entirely for x-ray examinations of poor patients.

(b) The Punjab Tuberculosis Association have made the following grants-in-aid during the present year:—Rs. 1,000 to Anti-Tuberculosis Dispensary, Jullundur, and Rs. 9,060 for equipment for the Rai Bahadur Gujar Mal Sanatorium, Amritsar.

(c) A care committee has been formed in Secunderabad under the Provincial Tuberculosis Association for facilitating treatment of tuberculous patients by giving monetary aid to them and to their families, if left unsupported.

The Union Mission Tuberculosis Sanatorium, Arogyavaram, Madanapalle, celebrated the twenty-fifth anniversary of its opening on 19th July, 1940.

Part of the Silver Jubilee celebrations was the opening of a fine Recreation Hall and Patients' Library costing about Rs. 20,000 without equipment. The hall which seats about 500 was built with donations given by patients, former patients and their friends and associated with the hall were the names of Dr. Dr. C. Frimodt-Möller whose connection with the sanatorium from its beginning is well known. Associated with the library was the name of Miss Gertrude Dodd, another of the tuberculosis pioneers of India whose donation was used for building the first sanatorium in South India out of which the Madanapalle sanatorium grew. The opening of the hall and library was performed by G. T. Boag, Esq., Chief Adviser to the Government of Madras, and at the public meeting in the hall Major-General N. M. Wilson, Surgeon-General to the Government of Madras, Dr. C. Frimodt-Möller, Medical Commissioner to the Tuberculosis Association of India, Rev. B. Rottschäfer, President of the Sanatorium, and Dr. P. Benjamin, Medical Superintendent, spoke. Grants were also given from the missions co-operating in the work of the sanatorium and from a great number of friends.

The third of the series of broadcast talks on 'Tuberculosis—A Menace to India' was delivered by Dr. C. Frimodt-Möller, C.B.E. (Hon.), Medical Commissioner to the Tuberculosis Association of India, from the Simla Radio Station on the 15th August, the subject being the 'Individual Defence against the Menace'. He said that the individual defence against the menace of tuberculosis in these days can be carried out far more effectively than before, not only in protecting the person against infection with tuberculosis, but even in securing restoration of health in many in whom the infection has developed to real and serious disease. The modern treatment has very much improved and many cases which 20 years ago would have ended fatally are now restored to live normal and healthy lives.

As defence measures against the disease, he laid stress on eating a well-balanced diet, on taking special care of health during certain periods of life (up to the sixth year and between the ages of 15 and 24), and after certain diseases.

**Central Advisory Board of Health.**—An important subject considered at the meetings of the Board at Poona in July last was the effect of housing and overcrowding on tuberculosis. It was agreed that while the rectification of defects in an existing slum area may be difficult, there can be no excuse when, after costly slum clearance by improvement trusts and other bodies, the cleared areas are permitted to be built over without due regard to the requirements of light, ventilation and sound hygienic construction. A strict enforcement of building by-laws in these circumstances is, therefore, an urgent necessity.

**Provincial and State Tuberculosis Associations.**—H. E. H. the Nizam of Hyderabad-Deccan has been pleased to sanction the construction of a tuberculosis sanatorium at Ananthagiri at an estimated cost of Rs. 12,50,000.

The Delhi Municipal Committee has decided to charge half fees for the vacant beds in the private cottages of the Silver Jubilee Tuberculosis Hospital during summer months.

**Tours.**—Major-General Jolly visited Calcutta and Indore at the end of August and discussed with the local workers anti-tuberculosis schemes and measures being taken for expanding their work.

#### CENTRAL ADVISORY BOARD OF HEALTH

At the meeting of the Central Advisory Board of Health, which took place in Poona in July, a number of subjects were discussed and decisions taken which, if acted upon, are likely to have a far-reaching effect on the health of the people of India. The Board, consisting as it does of the representatives of the Central and Provincial Governments and of the Governments of certain Indian States, is in a position to formulate health policy on lines which should secure wide acceptance in the country. Without co-ordination of effort between the numerous health authorities in India many of the country's problems, such as, for instance, control of infectious disease, cannot be solved successfully and the Central Advisory Board of Health, during the three years of its existence, has already proved its value as an integrating force in the campaign for raising the level of health of the people.

At this year's meeting the reports of two special committees appointed by the Board at its previous meetings to investigate the possibility of introducing compulsory inoculation of pilgrims against cholera and to study the complex questions associated with the prevention of food adulteration in India occupied a large part of the proceedings of the Board.

#### Inoculation of pilgrims

The Board, in adopting the report of the special committee appointed to examine the possibility of introducing a system of compulsory inoculation of pilgrims against cholera, considered that public opinion in favour of anti-cholera inoculation had grown in recent years and that the question of introducing compulsory inoculation could now be considered by

provincial and state governments without apprehension of any disturbing effects on the minds of the people. The Board recommended that provincial governments should select suitable centres in their areas and try out a scheme of indirect compulsory inoculation on lines successfully pursued by the Government of Bombay for the past four years in connection with the Pandharpur festival.

#### *Central Committee for Food Standards*

The committee on food adulteration had examined the problem from three aspects, viz (1) the technical, including food standards and technique of food analysis, (2) the legislative and (3) the administrative aspect. The committee has so far considered only the technical aspect of the problem and it is expected that its reports on the legislative and administrative aspects will be made available for the Board at its next meeting. The committee emphasized the fact that the improvement of methods of food analysis and the prevention of food adulteration in India will have to be a continuous process and that the establishment of co-ordination between the provinces is a matter second to none in urgency. With this object in view the Board recommended the appointment of a standing committee to be called 'The Central Committee for Food Standards' which would be in a position to advise the central, provincial and state governments on all aspects of food adulteration. Pending the establishment of the Central Committee the Food Adulteration Committee itself recommended all-India standards for 17 articles of food, while in respect of a number of other articles, the standards for which are a matter of controversy, the committee recommended that these should be investigated by the proposed Central Committee for Food Standards.

The existence of different food standards in neighbouring provinces and states at present interferes with the free flow of trade. The Central Committee should be in a position to suggest standards acceptable to all the governments concerned, thereby facilitating inter-provincial trade and a uniform enforcement of food adulteration laws.

Another important function of the Central Committee would be the issue from time to time to public analysts of 'instructions' incorporating the latest available information regarding methods of analysis. The standardization of methods is as important as the unification of standards of food purity.

Among other important decisions taken at this year's meeting of the Board, the following are of general interest:—

#### *Free laboratory service*

The importance of laboratory examination for the diagnosis of many infectious diseases cannot be over-emphasized. For instance, in regard to typhoid fever, the recorded statistics of mortality represent only a small fraction of the actual events. The diagnosis of typhoid fever cannot be done, in many cases, without laboratory aid. The provision of a free laboratory service to medical practitioners is essential for a successful campaign against this and many other infectious diseases. The value of such provision was demonstrated in Bombay during an epidemic of typhoid fever in 1938 when the Government of Bombay placed the services of the Haffkine Institute at the disposal of the medical practitioners of the city. In consequence many more cases were reported than had been experienced in previous years and the health authorities were able to locate with certainty the areas most affected and take effective measures against the spread of the disease.

The Board had before it a scheme for starting a provincial laboratory service which outlined a system of small district laboratories supported by regional laboratories for groups of districts and by a central laboratory for the province, which would co-ordinate the activities of the regional and district laboratories. The Board recommended this scheme for adoption by

provincial and state governments, with such modifications as local conditions may require.

#### *The health of school children*

There are numerous problems associated with the health of school children, for instance, the inculcation of healthy habits, provision for periodical medical examination and correction of the defects discovered during such examination, and the supply of adequate nutrition. It is generally accepted nowadays that systematic attention to the health of the children is an essential preliminary to any really remunerative system of instructions, whether it be in hygiene or other subjects in the curriculum. Further, teaching is not likely to be a success if the general school environment does not conform to reasonable hygienic standards. Before a considered policy can be drawn up and commended to the authorities concerned, much information has still to be collected as to the requirements of, and the progress already achieved in, different parts of India and the possibility of remedying the defects disclosed at the least possible cost. The Board therefore recommended that a special committee including educational experts should be appointed to report on the teaching of hygiene in schools, primary as well as secondary, rural as well as urban, the medical inspection of school children and their treatment and, in the primary educational stage, also on their nutrition.

#### *The effect of bad housing and overcrowding on tuberculosis*

There is abundant evidence available from countries where tuberculosis is prevalent, that unsatisfactory housing conditions and overcrowding tend to produce an increased incidence of the disease, while the transference of tuberculous patients from unhealthy to healthy dwellings produces an improvement in their symptoms and the physical signs of the disease. The failure on the part of the local bodies in many parts of India, to enforce the by-laws relating to health matters, has been a subject of constant reference in public health reports for a number of years.

### INDIAN CHEMICAL MANUFACTURERS' ASSOCIATION

#### *Press communique*

MEMBERS of the Indian Chemical Manufacturers' Association met Major-General G. G. Jolly, Director-General, Indian Medical Service, at the premises of the Association on 25th August.

The president welcomed General Jolly and others to the meeting. He referred to the activities of the Indian Chemical Manufacturers' Association as an all-India body since its inception two years before. He stated that the manufacturers of chemical and pharmaceutical products were in a position to supply most of the drug requirements of the country, but in starting new lines of manufacture they apprehended competition and dumping from abroad after the war. General Jolly then discussed with the members the requirements of the government in respect of medicines and drugs, and the possibilities of getting supplies.

Questions of the manufacturing and importing activities of the Indian Medical Stores Depôts and facilities for the manufacturers for making clinical trial of their products in government hospitals, were also discussed. General Jolly assured the members that there would be no unfair competition from the medical stores department. Mr. Lahiri, the president, thanked General Jolly and others for their kindness in attending the meeting of the Association. Among others present at the meeting were: Bt.-Colonel R. N. Chopra, Colonel J. R. Marriot (Controller of Supplies), Major S. P. Bhatia, Major-General P. S. Mills (Surgeon-General to the Government of Bengal) and Mr. A. F. MacCulloch (Chief Advisory Chemist, Medical Stores Department).

### THIRD ALL-INDIA OBSTETRIC AND GYNÆCOLOGICAL CONGRESS

The Third All-India Obstetric and Gynecological Congress will be held this year in Calcutta from the 27th to the 30th December, 1940—both days inclusive.

The subjects for discussion are:—

- (1) Anæmia of pregnancy;
- (2) Functional uterine hemorrhage; and
- (3) Maternity and child welfare.

For particulars please apply to the Joint Honorary Secretaries, the Bengal Obstetric and Gynecological Society, 91B, Chittaranjan Avenue, Calcutta.

#### PRIZE ESSAY

1. A gold medal called the 'Rai Shambhu Dayal Sahib Gold Medal' will be presented for the best prize essay on a public health subject to be announced each year.

2. The subject of the next essay is 'How can the public co-operate best with the Public Health Department in the prevention of diseases and the promotion of the health of the people'.

3. The competition will be open to the general public, including the medical and the public health workers in the United Provinces.

4. The essay is to be written in simple Hindi and should not exceed 3,000 words in length.

5. Essays should reach the medical officer in-charge, Provincial Hygiene Institute, United Provinces, Lucknow, by 15th November, 1940.

6. The name and address of the competitor must be distinctly written on each essay submitted and the envelope should have the words 'Prize Essay' in the top left-hand corner.

7. The director of public health, United Provinces, shall judge the merit of the essay and his decision with regard to the award of the medal shall be final.

8. No correspondence will be entered into on the subject of the competition.

9. No essay will be returned.

[The above notice was received on 25th September and was included in our October number at great inconvenience to ourselves; even this is ridiculously short notice, and very unfair on would-be competitors.—  
EDITOR, I. M. G.]

### THE PHARMACEUTICAL AND ALLIED MANUFACTURERS' AND DISTRIBUTORS' ASSOCIATION, LIMITED

In our note on p. 492 of the August number we mentioned seven 'members' of the association; this was due to a clerical error; the word should have been 'signatories' and it referred to the memorandum issued by the association.

There are in fact thirty-one founder members of the association and these include a number of Calcutta firms.

## Current Topics

### The Problem of the Virulence of the Bacillus of Koch

By ALFRED BOQUET  
and

### Le Probleme de la Virulence du Bacille de Koch

By A. SAENZ

(Abstracted from the *Bulletin de la Union Internationale Contre la Tuberculose*, January 1940, Vol. XVII, pp. 4-87.

THESE two papers on the virulence of tubercle bacilli were to be read at the XIth Conference of the International Union Against Tuberculosis which should have been held at Berlin in September 1939 but was cancelled because of the outbreak of war.

The two distinguished authors are well known from their investigations on the bacteriology of tuberculosis carried out at the Pasteur Institute, Paris, in the laboratories which until a few years ago were directed by the late Prof. Calmette, whose name is associated with the B.C.G. vaccine.

As the two papers deal with the same subject and their points of view largely coincide, it may suffice to treat them together. Whereas Boquet's paper reviews the field of recent work regarding the virulence of tubercle bacilli, A. Saenz presents his latest investigations. As the conclusions of the authors for a great deal are based upon these findings, a brief account may be given.

In order to elucidate whether different forms of clinical tuberculosis can be related to certain types of virulence, thirty-two strains from human tuberculous lesions were examined, some were derived from internal foci (sputum, spinal-fluid, pleural effusions, stomach-wash, pus, urine), others from superficial lesions such as tuberculoids of the skin (apart from lupus vulgaris), the patients representing active as well as inactive forms of tuberculosis. The virulence was determined

by subcutaneous inoculation into guinea-pigs of glycerine-potato cultures in doses from  $10^{-6}$  to  $10^{-8}$  milligrammes, the animals being sacrificed after 90 days. Twenty-nine cultures were of the human, three of the bovine type. All cultures were virulent, eighteen of the human strains having a 'normal' virulence, five being 'hypervirulent' and six slightly attenuated, while two of the bovine strains were 'hypervirulent', the third being normal. When the virulences were correlated with the different forms of clinical tuberculosis, no connection between highly virulent strains and severe forms of tuberculosis or between more attenuated forms and cases of inactive tuberculosis could be demonstrated; some of the most virulent strains were for instance derived from benign cases. e.g., from a tuberculous finger-joint, whereas attenuated strains could be isolated from severe cases of pulmonary tuberculosis. It may, however, be said that the difference in virulence do not seem to exceed the limit of variations as set by the technique employed. The term 'hypervirulent' also seems rather ambiguous as none of these cultures appear to have killed the guinea-pigs within three months, not even with doses of  $10^{-6}$  milligrammes. As all the strains described were able to produce generalized tuberculosis in guinea-pigs with doses containing from one to ten tubercle bacilli, they must all be said to have a standard virulence, thus confirming the common observation of earlier workers that strains from human tuberculosis generally show a remarkably high virulence without regard to the form of lesions, apart from cases of lupus vulgaris or other exceptional cases.

The fact that the majority of lupus strains are attenuated is also corroborated by Saenz who examined nineteen lupus strains and found that of seventeen strains of human type five were slightly, nine markedly attenuated and only three of normal virulence. Of two bovine strains one was normal, the other attenuated. These results are quite in conformity with the previous investigations in England, Denmark and Germany, the only discrepancy being, as Saenz himself points out,

that the French material contains an unusually low percentage of bovine types. This observation is in line with other investigations by Saenz.

Material comprising 903 strains submitted to type determination is presented here by Saenz who found the presence of bovine types in 22 instances, i.e., 2.43 per cent. This figure although not very informative in itself is remarkably low when the various sub-groups of the material are considered. Of 176 cases of tuberculous meningitis in children only nine were bovine; of 218 cases of stomach-wash in children one strain only was dysgonic although of human type, whereas among eight cases of cervical adenitis one strain was of bovine type. These groups are just those which in other countries present a remarkably high incidence of bovine infection, even as much as 80 per cent or more, as shown by A. S. Griffith in England and Scotland and by K. A. Jensen in Denmark. Saenz concludes therefore that the bovine infection in France is of considerably less importance compared with other countries. It should, however, be noted that the Saenz' material is not entirely unselected and, as the opposite is not stated, it must be presumed to cover an urban area. From Griffith's and K. A. Jensen's investigations we know that it is essential to search for the bovine infection in areas where cattle tuberculosis is common and where milk is not exposed to pasteurization or other heating devices. Saenz mentions an investigation from Northern France by Gernez who found three bovine cases out of 471 examined but he does not state whether these were rural or urban. Further investigations must be awaited with interest.

After these investigations which follow common lines, Saenz reports some experiments of a new character, from which the two French authors draw important conclusions as to the intrinsic nature of the pathogenicity of tubercle bacilli. Ten milligrammes of heat-killed bovine cultures were suspended in 1 c.c. of liquid paraffin and injected into the testicles of rabbits. The rabbits then developed within two months extensive pneumonic processes in the lungs, a large number of the animals even died spontaneously within 25 to 60 days. On autopsy the inoculated testicles were found to be transformed into large abscesses, some rupturing into the peritoneum and giving rise to lesions in the liver, spleen and diaphragm. The most striking observation was, however, the enormous changes in the lungs; these were enlarged, consolidated and contained large areas of caseous or necrotic pneumonia, many of the foci surrounded by marked hyperæmia. The changes were very similar to those seen in rabbits after intravenous inoculation of live, virulent bovine strains, even so much so that it would not be possible to distinguish between rabbits inoculated one way or the other. Rabbits inoculated either with liquid paraffin alone or with simple heat-killed bovine cultures show no pneumonic changes whatsoever. Heat-killed cultures of the human type inoculated into rabbits in a similar way, i.e., embedded in liquid paraffin and given intratesticularly, had also no effect, the only changes in the lungs being small scattered foci of no more importance than may be seen after intravenous injection of live human cultures. The fact is stressed by the author that the two conditions, the embodiment of the dead culture in liquid paraffin and the intratesticular mode of inoculation, are indispensable for obtaining successful experiments.

Even bovine cultures of extremely attenuated virulence, as the totally avirulent B.C.G. strain would do, when inoculated in the manner described cause similar vast changes in the lungs as would the heat-killed cultures of highly virulent, bovine strains. Saenz also states that avian cultures inoculated into rabbits in the same way cause the death of the animals within one or two months, no details, however, being given.

These experiments which Saenz himself very correctly, it must be granted, characterize as *les plus surprenant*, lead the authors to the conclusions that the pathogenic power of tubercle bacilli do not depend so much upon their viability, their ability to multiply rapidly in the host organism but rather upon some special chemical or 'physico-chemical' properties of the bacillary bodies.

These peculiar properties also determine the specific type of the bacilli, which might be dormant even if the virulence of the bacilli for some reason should have been depressed, as for instance with the B.C.G. strain which although entirely avirulent, according to the author, could produce major changes in the rabbits when inoculated in the way described.

It is of course not possible to pass any sort of judgment on these quite remarkable experiments at the present stage. It is much to be regretted that the outbreak of war prevented the conference taking place, thus depriving many eminent workers in tuberculosis from discussing this and other matters relating to the problem of virulence, one of the most fascinating and important problems in tuberculosis. It is, however, evident that more detailed and fuller reports besides confirmation from other laboratories of these thought-evoking experiments should be awaited before their real significance can be assessed.

J. F.-M.

## The Rehabilitation of the Tuberculous

By PENDRILL VARRIER-JONES

In a paper which was to be read before the XIth Conference of the International Union Against Tuberculosis Sir Pendrill Varrier-Jones very clearly discusses the problem of the rehabilitation of the tuberculous. He brings out into relief several facts about this important question. He believes that the fall in deaths and notification rates is deluding the world into the belief that tuberculosis is conquered, whereas in truth there is an increasing reservoir of infection. The cost of tuberculosis is increasing with prolongation of treatment. The tuberculous people are living longer, most of them in idleness and misery at the expense of the State. The faculties which the unfortunate victims of the disease possess are being completely wasted and no serious effort is being made to rehabilitate the tuberculous. In fact 'the whole anti-tuberculosis scheme fails if it fails to rehabilitate the tuberculous'.

In the absence of rehabilitation it is no wonder that sanatoria are largely occupied by patients who have returned in worse condition than before. Persistent failure to rehabilitate the patients also reacts upon the discovery of early cases. In the face of a complete dark economic future the patient and his friends avoid discovery till some terrifying symptom like hæmoptysis occurs—by which time the case is no longer early. It surely follows therefore that failure to adopt proper rehabilitation schemes is crippling the whole anti-tuberculosis effort in the world and that the principal beneficiaries of the present schemes are neither the patients nor the State.

The problem before the tuberculosis service is not only to restore the working capacity of the patients but to provide the tuberculous opportunities to earn;—'without opportunities to earn there is no rehabilitation'.

The author then discusses the question whether it is possible to rehabilitate the tuberculous and if so whom will it benefit. He quotes the example of Papworth where ex-patients and their families instead of receiving public assistance of £17,500 a year (which could only sustain them in disagreeable and depressing circumstances) earn under a system (in which work acts as a tonic for their health) £40,000 a year. These people pay £2,000 a year towards Unemployment and Health Insurance. The State therefore benefits by this scheme to the extent of £19,500 a year while the national economy has the purchasing power of £40,000 a year instead of £17,500. Such a scheme therefore 'benefits both the patients and the State'.

Sir Pendrill then traces the reasons for the delay in the development of rehabilitation schemes. In his view it is the apathy of the patients and of the tuberculosis service itself, besides the fact that the fit fear the competition of the unfit. The latter is to a great extent due to the nature of the world trade system which has linked world production to gold.



The solution suggested is to plan on a large scale 'both the care of the community and the patient has to be taken into account', and suggests that 'each Government should establish a National Rehabilitation Board: guarantee principal and interest on the capital sums required; regard the Board as potential contractor-general for all Government and municipal supplies, and as a matter of policy adopt rehabilitation as a preferable alternative to cash compensation. 'State Funds would be involved to the extent of the guarantee, and judging from the result at Papworth, the savings in other directions would more than cover any possible loss under this head. The Board could not at once undertake the execution of all Government orders but if in principle the Government would give preference to the Board it would not be long before a large number of unfit are rehabilitated.'

### The Value of Systematic Examination for the Detection of Tuberculosis in Subjects over 15 Years of Age

By H. BRAEUNING

(Abstracted from the *Bulletin of the International Union Against Tuberculosis*, Vol. XVII, April 1940)

PREVENTIVE examination in series of those living in close proximity to tuberculous patients is a well recognized method of detecting early cases of tuberculosis. In some countries this has been extended to the examination of homogeneous social groups like regiments, police, schools, colleges, factory workers, railway and tram employees. Finally the conclusion is reached that the whole population should be systematically surveyed. Is it possible?

In a paper which was to be read before the XIth Conference of International Union Against Tuberculosis Dr. Braeuning discusses the value of systematic examination in series of subjects over 15 years for the early diagnosis of tuberculosis. This special age group has been selected because in the area covered by the author's investigation, among several thousand cases of tuberculosis, less than 1 per cent were under 16, while 21 per cent of the dispensary population was under 16. The question has been discussed under three headings: (1) why does one undertake systematic examination for the detection of pulmonary tuberculosis, (2) will the progress of a tuberculosis campaign through early diagnosis of pulmonary tuberculosis be an adequate compensation for the trouble taken, (3) what systematic examinations are essential for the detection of pulmonary tuberculosis.

The author reports that x-ray examination of healthy persons showed that pulmonary tuberculosis starts almost always as a closed lesion and during the first year 15 per cent of cases develop open lesions. In his experience 70 per cent of all cases of open tuberculosis are detected at the stage of open lesions, i.e., normally too late. If the healthy population were x-rayed at least once a year this would enable almost all cases to be diagnosed before the stage of open lesions.

Figures are quoted to show that early detection of tuberculosis has a definite influence on the progress of the disease. According to the author 5 per cent of cases of pulmonary tuberculosis diagnosed within the first 12 months die from tuberculosis 1 to 2 years later in spite of treatment. The early diagnosis of these has no prophylactic significance. Approximately 15 per cent of all these cases of pulmonary tuberculosis heal without having become open even in the absence of any treatment. The early diagnosis of these has therefore no practical value. Between the two extremes in 80 per cent of these patients progress of the disease may be modified through our therapeutic efforts. Two groups of patients, one among the members of the hospital staff who, with two exceptions, conformed to medical orders and another from the general population in whom one-third did not comply with medical orders, have been compared. The hospital staff had 4 per cent severe lesions and no deaths; among the other patients 39 per cent had severe lesions and 32 per cent died. The author concludes 'that thanks to the systematic

examination of healthy subjects in view of early diagnosis of pulmonary tuberculosis, important results may be obtained'.

However, as approximately 5 per cent of cases of pulmonary tuberculosis die 1 to 2 years later in spite of treatment, the only absolutely safe protection against fatal tuberculosis is prevention of infection. Systematic examination in series are necessary as a safety measure against primary infection—in order to discover on the one hand cases who have not yet been infected, and on the other those who involve a risk of infection to their healthy neighbours. Systematic tuberculin testing can reveal what subjects had not yet been infected. Such an age group should be kept as far as possible away from the open cases. It would be useful to carry out x-ray examinations among associates of children under such an age, as this could give a clue to the sources of infection. As in infants, small children and during growth the primary infection often coincides with morbid symptoms, a systematic tuberculin testing would enable one to find out new patients when a conversion of a reaction which was negative until then is observed.

According to the author all subjects over 15 years of age as well as younger subjects who are exposed to infection should be x-rayed at least once a year. If it is impossible to examine such large numbers one should at least x-ray, (1) all cases exposed to tuberculous infection, (2) all groups who have special risks from their associates, (3) all groups who can be easily x-rayed, e.g., soldiers, students, (4) all suspect cases.

The comparative value of radiology, radiography and radiophotography in the examination of such large numbers is discussed. The best method of carrying out x-ray examination is to screen every case and then take a photograph in the position which reveals shadows ordinarily hidden by the cardiac and diaphragmatic shadows. In order to save time and money radiography is given up in systematic examinations, and less expensive methods like radiology or radiophotography are adopted. In the author's experience both these methods give an error of 2 per cent to 10 per cent as against radiography. Radiophotography has certain advantages over radiology in that it is less time consuming, the result is noted on a permanent record and is less expensive (as the work can be left to a less experienced assistant). If on the other hand one wishes to detect the smallest lesions, paper films are recommended. With a special condenser equipment some of the latest makes of these films are reported to give results equal to plates.

The author concludes that by such a systematic campaign one part of the problem can be solved. The treatment of all cases discovered in time, even before the appearance of any symptoms so as radically to reduce the rate of those who develop open lesions, and moreover the control of open cases is a much more arduous task. He expresses the opinion that only by legal measures will it be possible to secure systematic examination of all those who need it and the early and prolonged treatment of those who require institutional care, and he believes that timely diagnosis, early and intensive treatment and prophylaxis will bring about marked decline of the tuberculosis death rate within a few decades. However, as the measures are extremely radical and costly he advises their trial as an experimental measure in one or two centres of approximately 50,000 inhabitants, to ascertain if they can be carried out at the rate of 100 per cent and what results may be expected of them.

### Recognizable Tuberculosis in General Hospitals

By ROBERT E. PLUNKETT

and

EDWARD X. MICKOL

(Abstracted from the *American Review of Tuberculosis*, Vol. XLI, March 1940, p. 381)

DURING the last several years there have been many investigations in different countries which show that the

incidence of tuberculosis among nurses is several times higher than that among the females of the same age group in other occupations and that the incidence of tuberculosis infection as determined by tuberculin test increases with each year of service. This has been most marked when student nurses are in contact with known cases of tuberculosis as a part of their training and to a lesser degree it is found in hospitals where tuberculosis cases are not knowingly admitted.

Several studies in America showed that in some States 10 to 15 per cent of deaths from tuberculosis occurred in general hospitals who had no provision for the care of the tuberculous patients. Many of the terminal cases were admitted for non-tuberculous conditions and the correct diagnosis was only made some time after admission. In order to estimate the magnitude of unrecognized tuberculosis in general hospitals x-ray study was made by the authors of 4,853 adult admissions to fourteen general hospitals in ten cities of Upstate New York in 1937 and 1938.

Previous studies by x-ray examination of all consecutive cases admitted to certain hospitals and their out-patients over certain periods showed that 1.3 to 3 per cent of patients admitted to the hospitals and out-patients had significant chest disease not detected clinically, and that 0.3 per cent to 0.5 per cent had clinically significant pulmonary tuberculosis which would have been undiscovered. As the previous studies included children in whom significant re-infection type of infection is relatively uncommon, only patients 15 years of age and over have been included in the present studies.

In order to obtain a representative cross-section of the general population, the hospitals were selected from areas varying from 50,000 to 100,000 population and the actual selection of hospitals was done at random from the point of view of bed capacity and economic status of patients admitted. Each hospital was allowed 250 to 500 x-ray films (at the expense of the State Department of Health) depending on the total yearly admissions; and the patients examined formed 9.4 per cent of the total admissions in the participating hospitals in 1937.

Single flat films of the chest were taken of all patients of 15 years of age or over admitted (including private patients) but excluding those admitted to the tuberculosis section, known cases of tuberculosis, out-patient cases and those who were too ill to be disturbed for x-ray examination. These were excluded on account of administrative difficulties. Detailed study of all x-ray films was made with the help of the Tuberculosis Division.

One hundred and twenty-eight, i.e., 2.6 per cent of the 4,853 films studied, showed evidence of a re-infection type of tuberculosis. Fifty-one or 1.1 per cent showed characteristics of clinically significant lesions. The hospital records showed that in 24 tuberculosis was suspected by the attending staff and in the remaining 27 or 0.6 per cent of the total group, x-ray films revealed the first evidence of the disease, and those cases were fairly evenly distributed in the medical, surgical and obstetrical sections of the hospitals. The authors conclude that if similar conditions prevailed in other hospitals of the country, over 40,000 cases of unrecognized pulmonary tuberculosis were hospitalized during the year. When it is realized that in the general hospitals the usual nursing and prophylactic technique falls far short of the standard requirements for a tuberculosis institution, the state of affairs would mean an increased danger of transmission of infection to nurses and others by the hidden cases.

Moreover the studies reveal the possibility of utilizing the general hospital as an effective medium for case finding in tuberculosis. Finally the routine x-ray study of the adult population has also revealed unsuspected non-tuberculous thoracic conditions. The authors conclude that, diagnostically, x-ray is often essential. To be sure it is costly 'but human economy should be considered as important, if not more important than administrative economy'.

B. K. S.

## The Chemotherapy of Tuberculosis

By G. M. FINDLAY, C.B.E., M.D., D.Sc.

(Abstracted from the *Medical Press and Circular*, Vol. CCIII, 24th April, 1940, p. 348)

IN the chemotherapy of tuberculosis, efforts have been made to destroy the specific bacilli by stimulating the tissue resistance and by finding remedies that are directly bactericidal.

### CALCIUM SALTS

Numerous attempts have been made for more than a century, especially in France, to bring about recalcification of tuberculous tissues by the administration of calcium salts either alone or in association with vitamin D and parathyroid extract. Many cases of phthisis, however, show normal amounts of calcium in the blood and their treatment with calcium lactate causes no increase in the blood calcium. A different method of producing calcification has been suggested by Hunter and Hunter and Peill who inject into the lung gelatin impregnated with calcium chloride: 300 gm. of gelatin is dissolved in 900 c.c. of physiological saline and 100 c.c. of distilled water containing 50 gm. of calcium chloride is then added together with 0.5 gm. of acriflavine. After filtration and sterilization, injections of about 16 c.c. are given into the lung, the temperature of the mixture being about 80°C. Further evidence, however, is required of the value of calcium salts in stopping the spread of active tuberculosis.

The supposed value of cod-liver oil in tuberculosis also rests on a somewhat uncertain scientific basis. It was shown at an early stage that sodium morrhuate has no action in healing tuberculous processes in any way comparable to that of the chaulmoogric and hydnocarpic acids in leprosy. With the discovery that cod-liver oil has a high content of vitamins A and D, it was at first believed that in these vitamins lay the secret of the action of cod-liver oil. Unfortunately, the amount of vitamin D in the diet has no particular effect on tuberculosis. Vitamin A also appears not to have any direct action on the tuberculous process. A deficiency of vitamin A in the diet, however, causes keratinization of surface epithelium with a consequent decrease in the secretion of the epithelial glands. This secretion has both a mechanical action in removing, and perhaps a direct bactericidal action in killing organisms which may act as secondary invaders in open pulmonary tuberculosis. It is of interest to note that cod-liver oil has recently been successfully applied as a dressing for chronic infected conditions such as osteomyelitis. Cod-liver oil inhibits the growth of invading organisms and accelerates the regeneration of normal tissue. Although the active component is still unknown, crude is more satisfactory than purified cod-liver oil. Similar findings have been noted in the action of cod-liver oil in tuberculosis, so that possibly the same component that is active in osteomyelitis also plays a part in counteracting the secondary bacterial invaders in tuberculosis.

In view of the action of chaulmoogric and hydnocarpic acids in leprosy, their action has been tested in tuberculosis. Some improvement has been noted in lupus following intradermal inoculation of the ethyl esters of hydnocarpus oil to which has been added 4 per cent of creosote. Unfortunately the injections are attended by considerable pain and some local reaction. Intradermal injections of phenyl ethyl hydnocarpate, however, cause fewer reactions, and by this means Burgess has succeeded in healing localized patches in seven out of eleven patients. Similar results have been obtained by Wallace.

### SALTS OF THE HEAVY METALS

The action of a number of heavy metals has been tested on experimental tuberculosis in rodents. Arsenic, silicon and mercury have little or no curative action in animals, but a distinct retarding action has been reported by Walbum following injections of aluminium, barium, cerium, lanthanum, molybdenum, ruthenium, and selenium. Ferric chloride and didymium have also, it is claimed, a beneficial effect, while a bismuth-dye



preparation has some action in acute tuberculosis in rabbits; the only metals which have been used extensively, however, are cadmium, copper and gold. Cadmium in the form of an iodine-cadmium sulphide or glycine appears to stimulate the growth of fibrous tissue in animals. In man intramuscular injections of 3 c.c. of a 1 per cent colloidal cadmium suspension were found by Heaf to produce results in 27 cases quite equal to those of gold, with an almost complete absence of toxic reaction. Cornwall using either a 1 per cent cadmium sulphite in sterile olive oil or a 1 per cent colloidal cadmium sulphide, obtained alleviation of symptoms in only 13 out of 42 cases. Cadmium is, however, of such low toxicity that it can be used in patients with high temperatures and toxic symptoms.

When treatment by copper was first instituted, favourable reports were by no means infrequent but more recently doubt has been cast on its efficiency. Mercader, however, used a colloidal copper morphuate with good results in preference to copper benzoate and the various double compounds of cuprous cyanide of which cyanocuprol is the best known. Most interest has been aroused by the use of gold in tuberculosis. In the East gold has been recommended for many centuries in the treatment of disease, and its use in tuberculosis is mentioned in the Vedas as well as in the writings of Sushruta. In Western medicine its introduction is due to the alchemists who in their turn received it from the Arabs. In the sixteenth and seventeenth centuries it became so popular a remedy that Moliere in 'Le Medecin malgré lui' held it up to ridicule as capable of reviving the dead. The modern use of gold in tuberculosis dates from the observation by Koch in 1890 that simple gold salts such as the double cyanide of gold and potassium (KAuCy<sub>2</sub>) and gold chloride inhibit the growth of tubercle bacilli *in vitro*; gold chloride, however, failed to affect experimental tuberculosis in animals. Later, organic gold compounds were introduced. Krysolgan, the sodium salt of p-amino-o-auriomercaptobenzenecarboxylic acid, was found by Feldt to cause improvement in human tuberculosis, although it had little inhibitory action in animal tuberculosis. In 1924, Moellgaard, of Copenhagen, introduced the double thiosulphate of gold and sodium (AuS<sub>2</sub>O<sub>2</sub>Na), Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> under the name of crysalbine or sanocrysin. At first somewhat large doses were injected, but these frequently caused reactions not unlike those following the injection of tuberculin. It was thought that the reaction might be caused by endotoxins liberated by the disintegration of tubercle bacilli, and an antitoxic serum was therefore prepared for injection before the administration of sanocrysin; since the serum proved of little value its use has now been abandoned. To-day it is the custom to employ smaller doses of sanocrysin, particularly at first, though the amount may be gradually increased, for both animal experiments and clinical observations show that tolerance is slowly acquired.

After the introduction of sanocrysin other organic gold preparations were prepared for use (*cf.* table) in tuberculosis and also in rheumatoid arthritis. The gold compounds now on the market can be divided broadly speaking into three groups: (a) those soluble in water, (b) those soluble in oil, (c) those insoluble in oil. At first water-soluble compounds were largely employed, but at present oil-soluble preparations are preferred. Shrikande believes that oil-soluble preparations are less rapidly absorbed and less rapidly eliminated: their action is therefore more prolonged; the reactions following their use are rarer and the ease with which they can be injected is greater.

The most commonly used compounds are sanocrysin in oil and solganol B in oil (solganol B oleosum) given in weekly doses of from 0.05 to 0.1 gm., the total dosage not exceeding 1 gm.: when this amount has been injected an interval of at least twelve weeks should elapse before another course is given. A different dosage has been recommended in India by Banerjee. In febrile cases the first injection is 0.002 gm. of solganol B oleosum or sanocrysin in oil: this is increased by 0.002 gm., injections being given every four to

## ORGANIC GOLD COMPOUNDS

Chemical constitution	Proprietary name	Gold content (per cent)
Sodium and gold thiosulphate	Sanocrysin	37
	Crysalbine	
Sodium aurothiomalate	Myocrysin	50
Sodium aurothiopropionol sulphate and sodium thio-propionol thiosulphate.	Allochrysin	55
Sodium aurothiogluco-	Solganal B	50
Disodium p-sulphomethyl-amino-o-aurothiobenzenesulphate.	Solganal	36
Sodium aurothiosinamine benzoate.	Lopion	43
Sodium 2-aurothiobenzimidazole-4-carboxylate.	Triphal	47
Sodium p-N-dimethylamino-o-tolylphosphinate.	Aurophos	25
Sodium aurothiosulphate		
Sodium p-amino-o-auriomeraptobenzene carboxylate.	Krysolgan	50
Undisclosed (said to be a gold Keratinate).	Neosolganal	14

six days. In afebrile cases the initial dose is 0.01 gm. and this is doubled till 0.4 gm. is reached. A total of 5 to 6 gm. is administered.

When first introduced gold was somewhat indiscriminately given in every form of tuberculosis. Further experience has shown that the most suitable patients for chrysotherapy are those with recent exudative lesions. With discretion gold therapy may also be applied in cases of a chronic fibrotic type with acute exacerbations, and in those where it is desirable to collapse one lung by artificial pneumothorax and to check the progress of recent lesions in the other lung. When an affected lung has been collapsed gold salts have very little further curative action for, owing to its anæmic condition, the collapsed lung takes up little or no gold from the blood stream.

The value of gold salts can be judged by the disappearance of tubercle bacilli from the sputum, by the return to normal of both the red blood corpuscle sedimentation rate, and the Schilling differential leucocyte count, and by reduction of temperature and improvement in the body weight.

Although gold has now been in use for nearly sixteen years, opinions are still divided as to its true value in tuberculosis. In England, for instance, Peters and Short, as a result of controlled statistical investigations over a period of five years, concluded that among patients from sixteen to twenty-six years of age, chrysotherapy was of little value. On the other hand, in France, Bernard claimed improvement in approximately 50 per cent of cases, while in India, Banerjee obtained similar results in just over half of sixty selected cases. Against these good results must be placed the liability to toxic reactions. Although fever and erythema are not uncommon, severe reactions such as agranulocytosis, thrombopenia with purpura hæmorrhagica, aplastic anæmia, toxic jaundice, hæmorrhagic nephritis, and exfoliative dermatitis are comparatively rare. More especially in France nervous reactions have been reported of which the most serious is the possibility of a meningitis resulting from the activation and extension of a tuberculous focus. Gold salts should not therefore be administered to persons with tuberculous foci that might extend to the meninges or to those with renal or gastro-intestinal lesions. Recurrent attacks of hæmoptysis, great emaciation or fever with obvious toxæmia are also contra-indications. Large doses of vitamins A, B and C given before, during and after treatment are capable, it is claimed, of preventing a considerable number of the reactions due to chrysotherapy. The cause of the toxic reactions

seen in tuberculous patients treated with gold is still unsettled. Secher believes that many of the reactions are due to the liberation of toxins from the tuberculous lesions. The reasons for this view are that the frequency of the reactions depends not so much on the amount of gold administered as on the site of the lesions. In closed cases (pleurisy, fibrous tuberculosis, joint affections) where there is a likelihood of the absorption of liberated toxins, rise of temperature and erythema appear only in the first stage of treatment. On the other hand reactions in patients with open lesions are less common. Gold salts may give rise to conjunctivitis and phlyctenae, but phlyctenae can only be evoked experimentally by injecting gold salts into tuberculous animals. In tuberculous patients also the injection of gold salts may produce a hyperglycaemia similar to that following injections of tuberculin. Nevertheless, many of the reactions, such as agranulocytosis and exfoliative dermatitis, are not those associated with tuberculosis, but with poisoning by metals or metalloids such as bismuth, mercury or arsenic. Tuberculin injections in tuberculous patients

usually cause a rise in the red cell sedimentation rate, while gold salts produce no such change. The tuberculin-like action of gold cannot, therefore, be regarded as proven.

The action of gold in tuberculosis would seem to be due not to any specific bactericidal action on *Mycobacterium tuberculosis*, but rather to a stimulation of the reticulo-endothelial system, since gold is readily taken up by endothelial cells. Japanese workers have suggested that gold preparations are of value, not so much because of the gold they contain but because of the presence in the molecule of a sulphhydryl group in the form of an aurothio, thiosulphate or sulphite group.

The sulphonamide group of drugs in the hands of certain workers and in large doses has been found to have a retarding action on the development of tuberculosis in rodents, provided that the drugs are given at the same time as the infecting organisms. In tuberculosis in man, however, neither sulphanilamide nor sulphapyridine has proved to have any ameliorative action.

## Reviews

**MANSON'S TROPICAL DISEASES: A MANUAL OF THE DISEASES OF WARM CLIMATES.**—Edited by Philip H. Manson-Bahr, C.M.G., D.S.O., M.A., M.D., D.T.M. & H. (Cantab.), F.R.C.P. (Lond.). Eleventh Edition. 1940. Cassell and Company, Limited, London. Pp. xvi plus 1083, with 18 colour plates, 15 half-tone plates, 364 figures in the text, 6 maps and 28 charts. Price, 35s.

WAR is a great disturber of populations and no more appropriate moment could have been chosen for the publication of a new edition of what is undoubtedly the best textbook of tropical disease in the world.

It is most remarkably complete for a single-volume work on such a vast subject; none of the important diseases are skimped and few, if any, of the rare ones are left unnoticed. Further, the appendix on medical zoology will provide the average tropical worker with an efficient guide to laboratory work, which is such an essential part of practice in hot climates.

No radical changes have been made in this new edition, though additions and corrections have been made throughout, and despite careful pruning nearly a hundred pages have been added. This is in a way a tragedy, for, as we remarked in our last review, the thousand pages of the last edition was about the limit of reasonable size for a book of this kind; the present edition has 1083 pages, excluding thirty odd plates and half a dozen maps, and, though the binding is excellent, it seems doubtful if the book in its present form will stand up to four years' hard use as did the reviewer's copy of the tenth edition.

In the first chapter on life in the tropics there are some very wise observations. The author starts from the beginning, from Leadenhall Street or Mincing Lane, from the India or Colonial Office, and gives useful hints to selection boards sitting in the imperial capital. On the difficult subject of the suitability of an individual to life in the tropics, it is impossible to lay down hard-and-fast rules and any opinion expressed is sure to meet with a contrary one, for life in the tropics is far more varied than life in Great Britain; the candidate may find himself in the social whirl, if he has a fancy for whirling, of Singapore or Calcutta where he will make a greater number of friends of both sexes than he would at his local suburban tennis club, or he may find himself in the backwoods of Burma or in the West African bush where he will not meet another white man for weeks on end, or a white woman until he goes on his next leave. On the subject of alcohol the author is very cautious—and he need be. It would be interesting to collect data from those who have failed in the tropics through alcoholic excess; the

reviewer believes that a large number would be found to have been teetotallers before they came to the tropics, for it is the boy that has been brought up to take alcohol in moderation that is best armed against any temptation to take too much. It is not clear what the author means when he says 'On the whole, it may be said that the attainment of a certain degree of toughness, with a capacity for roughing it, together with that innate instinct of fending for oneself, which is so often exhibited in the hardy northern races, is a much more suitable preparation than the sheltered life enjoyed by many of the educated young people of the present day.'

Does he suggest that the 'hardy northern races' are not educated? Brave man, but would he repent this statement at the football club in Calcutta, for example? Anyway, whatever the author's meaning, the reviewer believes that 'breeding', admittedly a vague term, counts more than apparent 'toughness' in the tropics, and that the British prestige in the East would be maintained better were more attention be paid to 'social standing' in the selection of candidates for appointments in these countries. This last sentence is not as irrelevant as it might appear to be.

The new sections on diet and nutrition in the tropics is a welcome addition, as also is the emphasis the author has given to recent amenities which have changed the outlook of the European to life in the tropics, namely, the refrigerator and air conditioning; the former can be installed wherever a white man lives and will be found in many places where he doesn't, and the latter wherever there is electric current which means wherever there is a factory. Another new section is on tropical anemias; one might question the justification of including Cooley's anaemia in this category.

An excellent account of all the main diseases is given, malaria, trypanosomiasis, leishmaniasis, relapsing fever, filariasis, the dysenteries, plague, cholera, yellow fever, undulant fever, leprosy, schistosomiasis, etc., but the section on typhus seems a little confused—at least it had the effect of confusing the reviewer who thought that he had a fairly clear conception of this rather complicated subject. For example, the sporadic Brill's disease, which was only found amongst recent arrivals from European countries where epidemic typhus had occurred, is identified with endemic flea-borne typhus, and Maxcy's, Mooser's and other American investigators' work on this subject is not given its full implication. Further, Indian endemic typhus is uncompromisingly classed as tick-borne, whereas much of it is certainly not and conclusive evidence that any

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species of this insect was the vector in any single instance of this disease is lacking.

In his descriptions of the minor diseases the author seems a little less certain, though the majority of these are also very fair accounts in the space that he could afford for them. For the treatment of infantile biliary cirrhosis the reader is told that 'According to Green-Armstrong, when cases are seen early and parents are given the necessary instructions, recovery takes place in six to ten weeks', but he is given no clue as to what these instructions are, beyond taking the child from the mother and artificially nursing it. The section on bill diarrhoea wants a little fresh blood in it, as references to epidemics in Simla in the pre-bacteriological era can scarcely serve any useful purpose. This brings one to a real complaint, that is, the absences not only of references but of any indication of the historical period in which the authority quoted worked; for example, in this particular instance the author quotes Crombie as his main authority. The reviewer, having trailed through 26 volumes of *Cumulative Index*, eventually by pure chance discovered Crombie's paper in the *Indian Medical Gazette* of 1880.

Once more Dr. Manson-Bahr has defeated the gloomy prophets who have insisted that the time is past when one man can give a comprehensive account of tropical medicine as a whole. He has done it so often that he will probably be able to do it again, but what will he do about the next edition? In its present format the book will not take another hundred pages. Will he change the format? We hope not. The book at present is a 'handbook' and should remain one. Will he divide it into two volumes? We don't believe that this would be a wise move. So he will just have to use the blue pencil freely. We believe that this could be done without seriously impairing the utility of the book, but it will be delicate work for there is nothing obviously superfluous in this edition.

**THE INTER-RELATIONSHIP OF MIND AND BODY.**—The Proceedings of the Association for Research in Nervous and Mental Disease. (Volume XIX of a series of Research Publications.) Edited by F. Kennedy, Angus M. Frantz, and C. G. Hare. 1939. Volume XIX. The Williams and Wilkins Company, Baltimore. Pp. xx plus 381, with 28 illustrations and 10 tables. Obtainable from Messrs. Baillière, Tindall and Cox, London. Price, 36s.

THE present volume is the nineteenth contribution of its kind in the last twenty years. It contains contributions from twenty-four leading American psychiatrists who, each in his own way, deals with the problem of the mutual relationship of mind and body. In their contribution, entitled 'Hypnosis in Hysterical Hyperventilation', Drs. Mandel E. Cohen and Stanley Cobb inveigh against the employment any longer of such terms as 'physical and mental', 'organic and functional', 'somatic and psychic'. They admit that the terms 'neurological', 'psychiatric', 'psychological', 'anatomical', etc., have useful meanings to most people, since they indicate to what department or to what professor a problem should be taken. On the other hand, Drs. Cohen and Cobb emphasize rightly that these terms have no biological significance. They beg of us to put aside superstition, mythology, parallelism and other outworn creeds and to accept simply the fact that all stimuli which play upon one individual are physical, that all phenomena which take place in an organism are organic and that the psychological processes, although the most complex, are not exceptions to this postulate. There is no doubt that, thanks largely to American psychiatric research, this viewpoint will in time become basic to all medical science. Adolf Meyer's concept of psychobiology was largely responsible for the turn it gave to the concepts of psychological medicine. According to Drs. Cohen and Cobb we owe it to the pathological tradition of Virchow that medical students are still taught to believe that symptoms are caused by 'lesions' and

that if no 'lesion' is detectable, the symptoms presented must arise from some mythical process known as a 'functional' state, in spite of the fact that a function must be a function of some structure, unless, of course, we are prepared to invoke structureless supernatural agencies. The twenty-four essays cover a wide area of psychology and psychopathology including the Production of Somatic Disease by Emotional Disturbance, Emotional Behaviour Patterns in Animals, Electrical Activity of the Brain, Fetal Behaviour, etc. There is also an admirable collection of graphs and diagrams.

O. B.-H.

**NEW FACTS ON MENTAL DISORDERS: STUDY OF 89,190 CASES.**—By N. A. Dayton, M.D., M.C. 1940. Charles C. Thomas (Publisher), Springfield, Illinois. Pp. xxxiv plus 486. Profusely illustrated with graphs and tables. Price, \$4.50. Obtainable from Messrs. Baillière, Tindall and Cox, London. Price, 25s.

Of its kind this book is probably unique. It is not a study of separate individuals suffering from mental disorders but a statistical study of 89,190 cases viewed as a whole. The author states in his introduction that the book is not the product of the work of one person but of many. There were at one time twenty-four field investigators working in twenty mental hospitals and state schools. Office workers brought the total employed to thirty-five persons. The scheme was financed by generous grants in 1928, 1931 and 1938 from the Laura Spellman Rockefeller Foundation and the Rockefeller Foundation. The survey is grouped under ten principal headings:—Age in Mental Disorders; Nativity and Mental Disorders; Alcohol and Mental Disorders; Alcohol and Other Factors; Marriage and Mental Disorders; Marital Status and Other Factors; Clinical Diagnosis in Mental Disorders—Age; Clinical Diagnosis and Changing Incidence—Time Changes; Clinical Diagnosis and Other Factors. Are Mental Disorders on the Increase? This last section is perhaps the most interesting of all, because it tends to show that for a long time past a great deal of nonsense has been spoken and written on the 'increase of insanity'. As a matter of fact, the figures examined show that, as far as the State of Massachusetts is concerned, the number of first admissions into the state's mental hospitals is slowly increasing, but slower than the admissions for physical disorders, such as cancer, heart disease, arthritis, etc. On the other hand the constant demand for additional beds in mental hospitals can be attributed to (1) the long hospital residence of mental patients, and (2) a definite increase in the length of hospital stay. This latter cause the author considers is brought about by society being less able than formerly to absorb recovered patients, and changes are taking place in the recoverability of existing mental disorders in spite of advances in therapy. One learns that to escape a psychosis it is better to be a Catholic than a Protestant, but best of all to be a Jew. Likewise it is better to be married than single and worst of all to be divorced. The book is profusely illustrated with admirable graphs and tables.

O. B.-H.

**FORENSIC MEDICINE: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS.**—By Sydney Smith, M.D. (Edin.), F.R.C.P. (Edin.), D.P.H. Seventh Edition. 1940. J. and A. Churchill, Limited, London. Pp. xvi plus 680, with 179 illustrations. Price, 25s.

ANOTHER edition of this excellent book which aims at separating the essential from the non-essential in the matter of details has appeared after two years. Most of the points to which attention was drawn in our last review have been revised. The following deserve attention in the next edition: (i) Subgroups of A in blood groups and their inheritance; (ii) spelling of Hirschfeld (now spelt *Hirschfeld*) and Bagchi (now spelt *Bacchi*); (iii) completion of the series of slimming



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differs in many respects from the usual textbooks on this subject.

As is explained in the preface, the book is intended for the post-graduate who is familiar with the standard textbooks but desires at first-hand more practical help with the diagnosis and management of abdominal cases.

The main theme of the book, occupying two-thirds of the text, is the diagnosis and treatment of surgical dyspepsia. Surgical dyspepsia, it should be explained, signifies painful dyspepsia as distinct from medical, or painless, dyspepsia. The diagnosis of surgical dyspepsia is discussed at great length, and under such general headings as symptoms, mechanism of causation, ætiology, reflex dyspepsia, and so on. Later chapters in this section seek to define dyspepsia syndromes for certain particular diseases. Inevitably, in such a long discussion, chapters have been introduced here and there to enlarge upon certain points secondary, but necessary, to the main subject. In one such chapter the theories of the causation of peptic ulcer have been summarized, and it winds up with the suggestion that the practising surgeon should follow the theories of Virchow when engaged upon the preliminary treatment of his case, but should go over to the Aschoff camp when it comes to deciding on the type of operation to be performed.

A good description of gastroscopy is contributed by Dr. John Horan, and then comes the section on operative surgery, in which the *pièce de résistance* is the part dealing with the surgery of the stomach. Technique, especially suture work, receives great attention, and there must be few who will not find something useful among the many original ideas disclosed. The surgery of the other abdominal viscera is dealt with fully, but special mention should be made of the sections on appendicitis and carcinoma of the rectum.

The book deserves the attention of all practising surgeons, especially those who feel the need of something to help them refresh their clinical work and brush up their operative technique in times which make visits to the great surgical centres impossible.

W. McN. N.

**THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE ŒSOPHAGUS.**—By P. P. Vinson, B.S., M.A., M.D., D.Sc., F.A.C.P. 1940. Charles C. Thomas—Publisher, Springfield, Illinois. Pp. 224, with 98 illustrations. Price, \$4.00. Obtainable from Messrs. Ballière, Tindall and Cox, London. Price, 22s.

Every student of medicine is well acquainted with the names of Plummer and Vinson who provided much of the impetus for the present satisfactory management of lesions of the œsophagus. Many excellent articles have since been published on the subject by surgeons, physicians and endoscopists but they are not readily accessible to us, while the average textbooks deal with it rather inadequately from the practical point of view. It is, therefore, with some feeling that we welcome this unique monograph written by Vinson and justly dedicated to *late* Henry S. Plummer.

The book begins with general management of patients with dysphagia followed by a chapter on endoscopy. The author insists that endoscopic examination should be deferred as the last method of investigation. The various functional and organic disorders have next been dealt with. The descriptions are clear, concise and profusely illustrated.

Auscultation over the œsophagus while swallowing, formerly stressed as disclosing valuable evidence of obstruction, is now rarely employed in diagnosis. In about 40 per cent of the number of patients having dysphagia, obstruction in the œsophagus has been found to be due to carcinoma. Difficulty in swallowing solid food is usually the first symptom of œsophageal carcinoma. Dilated veins in the lower œsophagus may produce radiological evidence suggestive of a neoplastic change, but the former rarely, if ever, produce dysphagia. Plummer-Vinson syndrome has apparently been attributed to hysterical dysphagia. Nutritional disorders

including anæmia, glossitis, splenomegaly and/or achlorhydria, develop secondarily from an unbalanced diet because of the inability to swallow solid food from fear of choking. In this connection, we may say that there is a difference of opinion. For instance, Hurst attributed it to achalasia of the pharyngeal sphincter giving rise to mal-nutrition. Suzman, however, believed that dysphagia was merely a complication or concomitant manifestation of idiopathic hypochromic anæmia. Notwithstanding the fact that the œsophagus is relatively immune to formation of tubercle, a few interesting instances have been cited. In conclusion, a brief reference has been made to gastroscopy. There is a bibliography at the end of each section.

The book will prove useful to all those who are interested in œsophageal diseases.

R. C.

**THE ANATOMY OF THE FEMALE PELVIS.**—By F. A. Maguire, C.M.G., D.S.O., V.D., M.D., Ch.M., F.R.C.S. (Eng.), F.R.A.C.S., F.R.C.O.G. Third Edition. 1940. Angus and Robertson, Limited, Sydney. Pp. x plus 162. Illustrated. Price, 10s. 6d.

The majority of medical students—when their time comes for midwifery and gynaecological ward work—remember that most cynical of all mnemonics which begins:—‘Some inherit money.’

They remember that it stands for the branches of the internal iliac artery. They remember that urine flows under the uterine artery like water under a bridge. But that is about all they remember of the anatomy of the pelvis until it has been revised. *The Anatomy of the Female Pelvis* by F. A. Maguire is an excellent little book for this revision. It completely covers the female pelvis in 116 pages, it is easy reading and is well supplied with very good illustrations.

The bones, ligaments, muscles and fascia are first described and this is done well without too much detail. The supporting function of the levatores ani muscles is stressed by emphasizing their divisions, origins, and insertions. The obstetrician would like to see their function of directing the fetal occiput to the front indicated.

The urogenital diaphragm and vulva receive a conventional chapter each and the author goes on to take the pelvic viscera in general. In this chapter the three systems of viscera in the pelvis are described as having similar functions. Each has ducts of entrance—the pelvic colon, the ureters, and the fallopian tubes—each has a muscular elastic reservoir—the rectum, the bladder, and the uterus—and each has a canal of exit—the anal canal, the cervical canal and vagina, and the urethra. Their function is to receive, hold for a time and expel the fæces, fœtus, and urine, respectively.

The pelvic connective tissue is described and then the largest chapter in the book, 11 pages of text and 9 full-page diagrams, is devoted to the blood vessels and lymphatics.

The supports of the uterus are explained in fair detail. The author divides them into an upper set, the broad ligaments, the round ligaments, the uterosacral ligaments and the connective tissue sheaths of the neuro-vascular bundles, a middle set the levatores ani muscles, and a lower set the perineal body and the urogenital diaphragm. He lays great stress on the connective tissue sheaths of the vessels and nerves passing to the uterus, vagina and bladder. He describes these sheaths as passing from the lateral pelvic walls in the region of the ischial spines to the lateral walls of the cervix and vaginal vault. He compares them with the sheaths of the carotid, axillary and femoral vessels which certainly have little supporting function. Mackenrodt's ligaments, on which the undeniably successful Fothergill's operation depends, are not considered important by the author. He implies that they are a product of dissection. He states referring

to Mackenrodt's or the lateral cervico-pelvic ligaments. 'There is no doubt that dissection in a mass of connective tissue may display sheets of fibres running in various directions.' This is a view not generally accepted.

The various pelvic organs are next described separately and there is a good chapter on the applied anatomy of the female pelvis. The book is finished with an explanation of the pelvic examination of the female patient which should be helpful to the student. Inspection of the vulva, per vaginam and bimanual examinations, is described, and the reader told what to look for and how to recognize the abnormal.

A chapter on the nerves of the pelvis including the sympathetic would be a valuable addition especially in view of the work recently done on dysmenorrhœa, and a word here and there on development would add interest and help understanding and remembrance.

The illustrations, of which there are 35, are really good. It is a pity that it has been found necessary to use numbers in their description from another work. It makes it difficult and exasperating to find what each number stands for, especially as there is no order in the placing of the numbers below each diagram. All the numbers used are to be found in sequence in an appendix, but no one will wish to refer to this for the interpretation of each and every diagram.

G. B. W. F.

**SURGICAL ANATOMY.**—By Grant Massie, M.B., M.S. (Lond.). F.R.C.S. (Eng.). Fourth Edition. 1940. J. and A. Churchill, Limited, London. Pp. viii plus 472, with 158 illustrations. Many in colours. Price, 21s.

THE fourth edition of this well-known book is assured of a ready welcome. The text has been thoroughly revised with sundry additions, without however disturbing the balance between the anatomical and surgical subject-matter. The inclusion of numerous new illustrations and the replacement of nearly all the older x-ray plates have enhanced the value of the book. We have no doubt that the present volume will be found as useful as its predecessors. We strongly commend this book to the notice of medical students and their teachers. The printing, get-up and illustrations are all excellent.

P. N. R.

**STATISTICAL METHODS FOR MEDICAL AND BIOLOGICAL STUDENTS.**—By Gunner Dahlberg. 1940. George Allen and Unwin, Limited, London. Pp. 232. Price, 10s. 6d.

THIS is a book designed to serve as an elementary introduction to the methods used to ascertain the significance of biological data. It is suggested that with little mathematical equipment this book enables the research worker to dispense with the services of a statistician unfamiliar with the actual material to help him to interpret his results. The medical student and research worker will however find that considerably more than a little mathematical equipment is required to understand the book, and before they can hope to dispense with the services of a statistician the majority of research workers would have to employ such an expert to understand the mathematical formulæ given in this book. The text is in many parts too highly technical and this often defeats the end in view. Those who have the necessary mathematical equipment and are to some extent already familiar with the subject will find much of interest and value in this book.

C. L. P.

**AIDS TO INORGANIC CHEMISTRY.**—By R. G. Austin, B.Sc. (Lond.), A.I.C., F.R.M.S. 1940. Baillière, Tindall and Cox, London. Pp. x plus 348. Price, 5s.

THIS handy little volume belongs to the well-known Students' Aids Series and is designed to meet the needs of students of medicine, dental and veterinary surgery and pharmacy and also those of students of science. It does not pretend to be a complete textbook of the

subject, but is intended for use by students who have already attended lectures on inorganic chemistry. The various chemical reactions have been explained by equations and, where possible, simple interpretations of the mechanism of the reactions have been given prominence in order that students may gain some insight into the principles of chemical change and so minimize the memorizing of long equations. The most interesting feature of the book, very useful to students of medical and allied sciences, is the paragraph on the physiological action under each of the common inorganic compounds described. The book has been written in a clear style by a teacher of wide experience and should prove very valuable for those who have no time to go through the larger textbooks on the subject.

S. G.

**PREVENTION OF VENEREAL DISEASE.**—By Marie C. Stopes. Third Edition. 1939. Putnam and Company, Limited, London (42, Great Russell Street, W.C.1). Pp. xi plus 62. Price, 2s. 6d.

THIS is a useful little book written in Dr. Stopes' direct and lucid style. The author's aim is, as always, to tell the facts to those who most need to know them. The book will serve a very useful purpose and should be widely read.

**BIRTH CONTROL: WHY, WHEN AND HOW?**—By B. L. Raina, M.B., B.S. Second Edition. New Book Company, Bombay (Hornby Road, Fort). Pp. 63. Illustrated

A BEGINNING has been made. The scheme has yet to be extended and adapted to Indian conditions, climatic, economic and social.

S. D. S. G.

## Abstracts from Reports

### ANNUAL REPORT OF THE KING EDWARD VII SANATORIUM, BHOWALI, U. P., FOR THE YEAR 1939

THE sanatorium remained open throughout the year and the accommodation available for the general public was occupied except during the winter months and, as usual, there was a waiting list during the season, especially for the lower classes.

Seventy-one patients remained in the sanatorium on 1st January, 1939, from the previous year and 227 patients were admitted and 228 discharged during the year under report. The daily average number of patients treated was 113.44, the largest number being 145 during the month of June and the lowest 69 in the month of January 1939.

Eighteen beds out of 150 are endowment beds reserved for the nominees of the donors and 132 beds only are therefore available for the general public. The sanatorium is, however, grateful to the donors for their standing permission to utilize their beds, when available, for use of the general public.

'B' class cottages are convertible into 'A' class accommodation. For these reasons the actual strength of patients may sometimes be less than the accommodation available.

#### *Building work and improvements:—*

The construction of the following buildings was taken in hand during the year.

*A block of six kitchens for patients of the 'C' class.*—The existing kitchens were at some distance from 'C' class block no. 2, and caused inconvenience to the patients who consequently showed unwillingness to occupy the block. New kitchens were therefore constructed close to the patients' block, out of the material obtained from dismantling the servants' quarters which were in front of and close to the administrative building and looked very unsuitable on their present site. The old kitchens were converted



'Elastoplast' applied to Impetigo.

2



An 'Elastoplast' Boil Dressing.



Fig. 1 (Bed Sore). Cleansing surrounding area before treatment.



Fig. 2 (Bed Sore). 'Elastoplast' applied.



Fig. 3 (Bed Sore). After eight weeks.

# 'Elastoplast' in the treatment of common skin lesions

## IMPETIGO (See First Illustration).

Crusts and pustules are not removed but are covered with a strip of 'Elastoplast' Bandage or Plaster without any intervening dressing.

## BOILS (See Second Illustration).

'Elastoplast' Boil Dressings (Medication: Mercury and Carbolic) may be applied, or alternatively, two or three layers of ordinary 'Elastoplast' form a very effective treatment. 'Elastoplast' splints the inflamed area, and protects the boil from counter-irritation.

## BED SORES (See Figs. 1, 2 and 3).

The lesion is cleansed and dried and covered with a single or, preferably, double layer of 'Elastoplast,' without any intervening dressing and *without stretching the plaster*. It is left undisturbed as long as comfortable.

## BURNS

The immediate and direct application of 'Elastoplast' (unstretched) to burns and scalds of the first or second degree provides an artificial scab, allays pain, forms a convenient and comfortable dressing; and, if left undisturbed for 7 to 10 days (provided neither unusual pain nor rise in temperature be experienced), healing results without any other or further application.

## BLISTERS

'Elastoplast' is applied over the threatening blister, or after piercing if the blister has formed. Immediate relief from pain is obtained and infection of the blister is prevented.

# Elastoplast

TRADE MARK BRAND

## THE MODERN SURGICAL DRESSING

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Made in England by T. J. SMITH & NEPHEW, LTD., HULL.

'Elastoplast' Bandages and Dressings are specially prepared for use in the Tropics

# KEEPS FALSE TEETH CLEAN

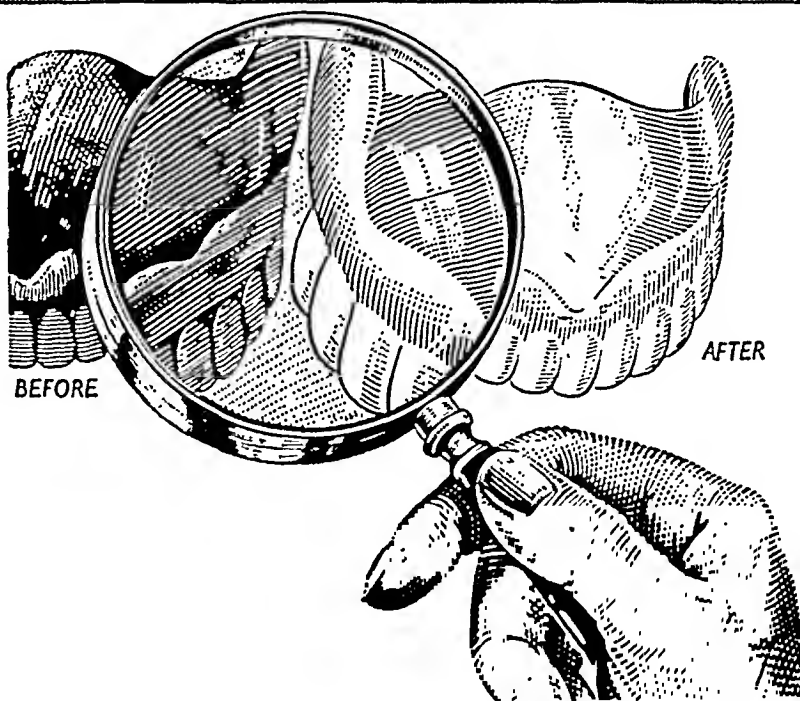
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"I really think in all my experience that 'Steradent' is the finest product I have used" writes a leading dentist. It is widely acknowledged by the Dental Profession to be the most efficient preparation for cleaning and sterilising dentures. It removes mucin film, tartar, stains, tarnish and all unsanitary accumulations. It is harmless to gold, platinum, stainless steel, etc. Patients should immerse their dentures overnight in a glass of warm water in which 'Steradent' has been dissolved. Then take out and rinse.

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# Steradent

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into servants' quarters. All these changes were brought about at a cost of about Rs. 1,800.

*Dining room and kitchen for female nurses.*—There was no common dining room for the nurses, who consequently had to take their meals in their own rooms. A dining room attached to the nurses' quarters and a kitchen close by were constructed at a cost of about Rs. 1,200.

*Incinerator and fuel shed.*—Owing to the larger number of patients admitted during recent years, the necessity of an additional incinerator was keenly felt, and this was constructed at a cost of about Rs. 500.

Besides the above construction, certain additions and alterations of minor importance to some of the existing buildings were done, with the idea of improving the general appearance of the institution and at the same time giving greater comfort to the patients. For instance, the open ward of the Red-Cross block was closed in by partially glazed and partially gauzed doors to enable the patients to live with comfort during the winter months. Such improvements are, however, too numerous to mention and are difficult to describe in detail.

*Police ward.*—The outstanding construction during the year under report was a ward of 12 beds for patients of the police department. The ward has been constructed from donations received from members of the U. P. Police Service as a memorial to Mr. G. W. Cole, I.P., Superintendent of Police, and Sub-Inspector Jainti Prasad, who lost their lives in an encounter with an armed murderer in the Farrukhabad District on 3rd April, 1936. The whole building consists of a hall with open verandahs in front and behind, and a ward-boys' room attached to it. The ward was opened by R. A. Horton, Esqr., C.I.E., Inspector-General of Police, U. P., on 8th October, 1939.

*Post-graduate training:*—

Six medical men came to the sanatorium for post-graduate training during the year under report.

*Social functions:*—

The 'Sanatorium Day' was celebrated on 13th and 14th May when a number of sports and competitions in indoor games were held.

A number of small tea-parties were also arranged by certain patients and they helped to brighten up the sanatorium life, giving those who participated in them a chance to forget their ills and infirmities for the time being.

The medical staff were 'at-home' to all other members of the staff and to the patients and their attendants on 20th June.

*Library:*—

The Editors of the *Hindustan Times* and *National Herald* stopped sending free copies of their papers owing to war conditions for which we are sorry. We are very grateful to the Editors of the *Statesman*, *Pioneer* and *Illustrated Weekly of India* for continuing to supply free copies of their papers in spite of the difficulties created by the war. Horlicks Limited continued supplying free copies of the *Sphere*, *Strand* and *Tit Bits* and their generous gift is gratefully appreciated. It has to be mentioned with the greatest regret that Horlicks find themselves unable to continue the gift of the three newspapers during 1940 owing to war conditions.

*My Magazine of India* published from Madras was added to the list of free copies during the year under report, and the Editor deserves thanks for the gift. One of our ex-patients presented a free copy of the *Orient*, an illustrated weekly from Calcutta, in appreciation of his recovery in the sanatorium.

The sanatorium subscribed to the following newspapers and periodicals, in addition:—

Hindi—*Arjun*, *Madhuri*, *Chand* and *Kalyan*.

Urdu—*Tej*, *Humaun* and *Nigar*.

English—*The Pioneer*, *The Leader* and *Modern Review*.

*Our most urgent need:*—

The most pressing need at the present moment is electrification of the sanatorium, the urgency of which

has been shown in the reports for the last two years. It was suggested in last year's report that 'the Government can either persuade the Naini Tal Municipal Board to supply the electric current or sanction a non-recurring grant to the sanatorium for having its own high tension line'.

The Hon'ble Mrs. Vijaya Lakshmi Pandit, Minister of Local Self-Government and Health, paid her first official visit to the sanatorium in the month of May 1939, and observed that 'the sanatorium urgently requires electricity for light without which the x-ray plant is not able to function in a satisfactory manner' and she expressed the hope that the difficulty will soon be remedied.

It must be acknowledged with gratification that since the visit of the Hon'ble Minister to the sanatorium, the Government have taken interest in the matter of electrification of the institution and is favourably considering the question of making a non-recurring grant to meet the cost of laying the high tension line from the Municipal Power House at Naini Tal to the sanatorium. The Government has even gone to the length of ascertaining through the Deputy Commissioner in-charge of Kumaon Division the views of the Municipal Board and pointing out to them that the Eastern Command having shifted from Naini Tal, they ought to welcome the new outlet for their electrical energy.

It is earnestly hoped that the Municipal Board will not try to bargain with the Government in a commercial spirit as they have done with the sanatorium, but will show a spirit of co-operation and compromise by agreeing to supply the current at reasonable rates if the high tension line is laid from the non-recurring grant which the sanatorium expects to receive from the Government for the purpose.

## TUBERCULOSIS AMONG INDUSTRIAL WORKERS

In the course of investigations into the relation of tuberculosis to industry, an examination of over 3,000 workers showed that over 80 per cent of the workers are drawn from distant rural areas and that there is a high incidence of infection and disease among them states the annual report of the All-India Institute of Hygiene and Public Health for the year 1939. Investigation of over 900 children belonging to the same group showed an incidence of infection in about 68 per cent and disease of lungs in about 12 per cent.

Active research has been pursued into various conditions of nutritional deficiency. Methods have been developed for detecting such conditions in their initial stages. One of these methods is the development of an apparatus, the visual photometer, which has been successfully used in sectional surveys of the population.

In view of the widespread vitamin-A deficiency among the population as shown by surveys, the extensive studies of the vitamin-A content of the liver oils of locally available fish were undertaken. It was found that many of these oils were even richer than imported cod-liver oils in their vitamin content. As the difficulties in the import of foreign fish liver oils are increasing every day, a strong plea is made for the encouragement of the local fish-liver oil industry.

## ANNUAL PUBLIC HEALTH REPORT OF THE PROVINCE OF ORISSA FOR THE YEAR 1938

*Provincial birth and death rates.*—The provincial birth rate for the year 1938 was 33.8 per mille as against 34.8 in 1937 and death rate was 29.5 in 1938 as against 28.6 in 1937. Thus the birth rate in 1938 showed a decrease of 1.0 and the death rate an increase of 0.9. This lower birth rate is probably due to some amount of agricultural distress brought about by the heavy recurring floods and the increase in the incidence of malaria in 1938.

*Cholera.*—Although the province is notorious for cholera, it remained almost free from the disease during the year, compared with the previous years. The total



number of deaths recorded from cholera during 1938 was 1,309 as against 7,977 in 1936 and 5,076 in 1937.

**Smallpox.**—The total number of deaths recorded from smallpox during the year 1938 was 3,321 as against 2,269 in 1937 and 3,780 in 1936 giving a mortality rate of 0.5 as against 0.3 in the previous year.

**Plague.**—No case of plague was reported during the year. The port of Rangoon which maintains direct and constant shipping communications with Orissa through its port of Gopalpur remained infected with plague almost throughout the year, and consequently steps had to be taken at the port of Gopalpur for carrying out all necessary measures.

**Dysentery and diarrhoea.**—There were 19,816 deaths from this group of diseases during the year 1938 as against 17,194 in 1937 and 16,283 in 1936 and the mortality rate was 2.8 as against 2.5 in 1937 and 2.3 in 1936.

The epidemiology and the high incidence of these diseases have probably some relationship with high humidity in the low-lying coastal districts where they are most marked, and like some other diseases they seem to follow a curve of periodicity. To a large extent they are, like cholera, directly associated with inadequate and bad drinking water-supply and defective sanitation in the rural, and to a less extent in the urban areas. The recurring floods no doubt also play an important part in bringing about such a bad state of sanitation.

A careful study of the facts relating to bowel diseases indicates that the chief measure for their mitigation and prevention is the provision of adequate and wholesome water-supplies for drinking in the rural areas. Where protected water-supplies have been given, as in the Puri municipality, the incidence of these diseases has become remarkably low when compared with the condition before it was introduced.

**Respiratory diseases.**—Four thousand nine hundred and sixty-seven deaths were recorded from respiratory diseases during the year giving a mortality rate of 0.7 which is higher than the mortality rate from smallpox. Deaths from pneumonia and pulmonary tuberculosis, which are included, probably claim quite a big percentage of the total deaths recorded under this cause. In this connection it may be said that provincial and district tuberculosis associations have been formed and attempts are being made to organize a campaign against tuberculosis to start with in the provincial headquarters town of Cuttack, by establishing a model clinic.

**Fevers.**—The death rate under the general head 'fever' was 16.0 during the year 1938 as compared with 15.2 in 1937.

Malaria was prevalent throughout the province in more or less epidemic form during the year.

Colonel G. Covell, I.M.S., Director, Malaria Institute of India, visited the province in September 1938. He visited three localities in which the malaria problems of the province were considered to be particularly urgent, viz:—

1. Chatrapur and the portion of Ganjam district which lies between Gopalpur on the sea coast and Rambha on the shore of Chilka lake.

2. Kendrapara, a municipality in the deltaic region.

3. Chandipur in Balasore district, the headquarters of the Proof and Experimental Station of the Military Department.

After the short investigation which he made he was of opinion that the malaria problems of the province are both extensive and varied and that practically nothing is known as to the anopheline vector responsible for the transmission of malaria in different parts of the province or of the factors determining the occurrence of epidemics of the disease. He was further of opinion that in order to tackle the malaria problems with any hope of success preliminary observations by a unit composed of trained personnel is necessary. To this end he recommended the deputation of a research unit belonging to the Malaria Institute of India to be

located in the first instance in one of the villages on the shore of the Chilka lake.

Quinine worth Rs. 2,772 was sold through post offices and other vendors during the year under report. Thirty-six pounds of quinine sulphate costing Rs. 648 out of the Government of India stock was distributed free in the malaria-affected areas of the province.

**Fairs and festivals.**—The most important and famous among these are the *Snan* and *Rath Jatra* festivals which are held at Puri. They attract a large number of pilgrims from all over India. In 1938, the *Snan Jatra* was held on the 12th June, the *Rath Jatra* on 29th June, and the Return Car festival on the 7th of July. The festivals were attended by about 52,000, 83,000, and 79,000 pilgrims respectively. As usual a large number of pilgrims halted in the various dharmasalas and lodging houses. Some stayed with friends and many camped on roadsides, while a large number assembled only for a day. Special sanitary arrangements were made from the 10th June to 9th July.

All the public wells were cleaned of silt. Preliminary disinfection of private and public wells including those in the lodging houses and dharmasalas 10 days before the festivals was carried out. Subsequently, during the festivals all the public wells and those in the large lodging houses and dharmasalas were heavily disinfected from time to time so as to make the water distasteful and thus prevent people from using them for drinking. Discarding the overchlorinated wells in the lodging houses where piped water-supply had already been installed, all the wells in the other lodging houses and private houses were 'phaged' every alternate day and whenever thought necessary.

For 30 days, from the 10th June to the 9th July, arrangements were made for a continuous piped water-supply for 24 hours in the town as another measure of special facilities and precautions.

The important tanks regarded as sacred were disinfected as often as necessary and people were prohibited from collecting and carrying water from these tanks for drinking purposes. Arrangements were made through the respective health authorities of the railway and the Puri district board to treat the sources of water-supply with bacteriophage at the nearest railway stations and along the Jagannath trunk road including the pilgrim centres at Sakshigopal and Bhubaneswar. Special mention may be made of the compulsory provision that now exists that all lodging houses should have protected pipe water connection before licences to these places are granted.

As regards control over food supplies during this festival careful inspection of all the shops that dealt in articles of food was made regularly not only by health inspectors, but also by the medical officers in charge of respective wards. A vigilant watch was exercised to see that the foodstuffs were fresh and wholesome and protected from dust and flies. Such articles as were found unwholesome or adulterated were destroyed. It is satisfactory to note that most of the shop-keepers and vendors of foodstuffs fully co-operated with the health staff in the efforts made to prevent infection occurring and spreading through articles of food and drink.

Puri is a place of pilgrimage and the temple *Mahaprasad* is the main source of food supply for more than 90 per cent of the pilgrims. The temple authorities are solely responsible for the control of sale of such foodstuff.

Although there were stray cases of cholera in the town earlier in the year, since March, and the interior of the district reported a large number of cases prior to the commencement of the festival, it fortunately did not assume epidemic form during the actual festival period, thanks to the measures taken by the district board. A few cases of purging and vomiting occurred but the situation was never alarming and was checked at once. There were 44 attacks with 3 deaths. None of these cases that died was inoculated.



# The Influence of Virol on the Growth of Children

*A Summary of Investigations\* published in the  
"Medical Officer," March 30 and April 6, 1935*

A NUMBER of children, all receiving their customary home diet, were given either No Supplement, Cod Liver Oil, Halibut Liver Oil (with milk to provide equal calories) or Virol. The experimental scheme provided that each child should have a period on each treatment in turn, in such a way that every possible sequence was included. Rigid statistical control was thus possible.

## Gain or Loss in Weight on Various Supplements:—

Supplement	Total gain in ozs. over all periods	Average gain per child per week in ozs. over all periods	Total loss in ozs. during summer period only	Average loss per child per week in ozs. during summer period only
No Supplement - -	88	0.3	— 103	— 1.4
Cod Liver Oil - -	287	1.0	— 77	— 1.1
Halibut Liver Oil with milk - - -	333	1.2	— 184	— 2.6
VIROL - - - -	762	2.6	— 7	— 0.1

Whereas earlier investigations had shown that the mere addition of vitamins had no effect on growth, these investigations have conclusively proved that Virol—a balanced food containing all the necessary vitamins—has a definite and remarkable effect in bringing the rate of growth up to the recommended standard. Virol was the only one of the supplements used that promoted this ideal rate of growth.

Virol was the one and only preparation that maintained the children's weight in the hot weather.

\* The full report will be sent on application to Messrs. A. H. Wheeler & Co.,  
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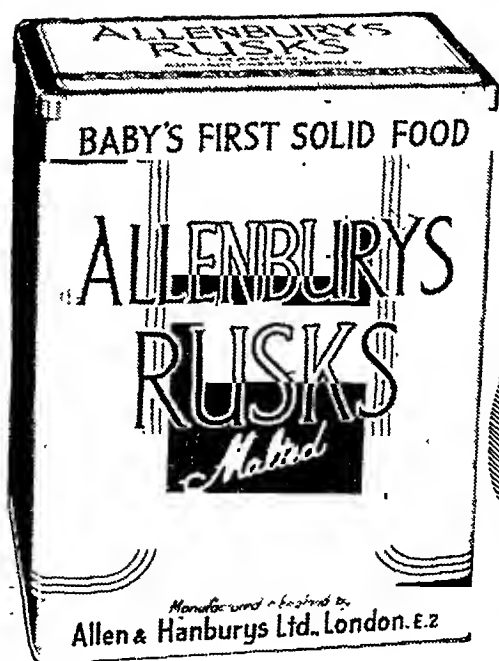
# Baby's First Food

Allenburys Malted Rusks are a valuable food from the age of ten months onwards, and may be used even earlier as a stimulus to salivary secretion and a help to teething. Their use encourages the development of a strong, wide jaw in which there is ample room for the teeth.

Vitamin D (calciferol), in the form of irradiated ergosterol, is added to the Rusks in the process of manufacture, in order to ensure normal calcification of bones and teeth.

The Rusks retain their crispness and flavour under the most varied climatic conditions.

In tins containing  $\frac{1}{2}$  lb., 1 lb., 2 $\frac{1}{4}$  lbs.



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## Correspondence

### MADRAS MEDICAL REGISTER, 1940—COMPILED AND PUBLICATION OF CHANGES OF ADDRESSES OF MEDICAL PRACTITIONERS

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—It was observed in the course of the recent elections to the Madras Medical Council as well as the Medical Council of India that the addresses of a large number of registered medical practitioners were either out of date or not known, with the result that an unexpectedly large number of voting and other papers were returned to this office. In order that the addresses of medical practitioners may be correctly recorded in the annual Madras Medical Register, not only for the purpose of elections, but for the general advantage of the medical profession, I request you kindly to invite the attention of the medical practitioners through the columns of your valued journal to this fact and to suggest that not only their present addresses but also the changes in their addresses, as soon as such changes occur, should be intimated to the Registrar, Madras Medical Council, in the form shown below:—

1. Registration Certificate No.....
2. Name as in the Registration Certificate.....
3. Present (or change of) address:.....

Yours, etc.,

H. S. HENSMAN, O.B.E.,  
M.R.C.S., L.R.C.P.,  
Registrar,  
Madras Medical Council.

100, MOUNT ROAD,  
CATHEDRAL P. O.,  
MADRAS,  
29th July, 1940.

### LOWERING OF INSURANCE FEES

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—It has come to my knowledge that some of the Insurance Companies are paying only Rs. 5 for examination of cases when, as a matter of fact, the legal fee for the same, as allowed by majority of Companies is Rs. 6 or Rs. 8 per case up to Rs. 2,000. Therefore I would request my fellow practitioners to charge not less than Rs. 6 for each case. If the Companies do not pay their scheduled fees, the examination of cases of such Companies should not be made as this would lead to illegal lowering of the fee day by day. In the interest of us all I make this appeal and hope that the medical licentiates who do insurance work will kindly respond to it.

Yours, etc.,

K. C. MISSRA, L.M.F.,  
Bhabua Missra Dispensary.

BHABUA,  
19th August, 1940.

### THE RANGE OF THE MALARIA-CARRYING MOSQUITO

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—Although the range of the mosquito has frequently been a subject of scientific investigation, statements made in the past have often been based on pure speculation, therefore any positive evidence on the range of malaria-infected mosquitoes is a practical point that seems worth recording.

Stephens and Christophers (1902, *Rep. Malaria Committee*, Roy. Soc., 7th Ser.) investigating *Anopheles culicifacies* failed to find mosquitoes 600 yards from

extensive breeding places. This observation has been confirmed by more recent investigators and it is generally acknowledged that the flight of this species is limited to half a mile. Afridi and Majid (1938, *Journ. Mal. Inst. India*, I, 155) investigating the *Culex fatigans* nuisance in Delhi found marked specimens of this species a maximum distance of three miles from their point of release; there was however strong evidence that the flight was carried out in stages.

*Aedes aegypti* is essentially a domestic mosquito and seldom strays more than 100 yards from its breeding place.

In most of the investigations on this subject, overland flight has been considered where the possibilities for resting en route were innumerable, but the general impression conveyed in textbooks is that about a quarter of a mile is the maximum range of direct flight and that if a ship is moored a greater distance than this from the shore the occupants will be safe from mosquito-borne diseases, e.g., malaria and yellow fever.

The following incident indicates that there may be exceptions to this rule.

I was recently a passenger on a ship bound for Colombo (and beyond). We sailed from Southampton leaving at night; we sighted no land until we arrived at 'A' on the 10th evening where we stayed until the 12th morning. We were moored over a mile from the shore (this statement was confirmed from the bridge); the harbour was crowded and we had at least two large ships between us and the shore. A large oil lighter lay alongside us for one night and the boat was visited by many country craft and small motor boats. No passengers were allowed ashore at 'A'. I was told that it was the height of the malaria season. We next called at 'B' on the 14th; the ship was again moored at least a mile from the shore, but on the 14th evening we called at an island, 'C', and took on water; here we lay within about 600 yards of the shore.

On the 29th day of the voyage, I was asked by the ship's surgeon to see a passenger in consultation. He was a young man, aged 21, who had never left England before; he had first felt ill on the 23rd, on the 25th he was admitted to the ship's hospital with a temperature of 102°; he was slightly better next day but on the 27th his temperature rose again and he vomited, it fell to 100° on the 28th but on the 29th it rose to 102° and he vomited again. He had no rigors but he sweated profusely when the temperature fell. His tongue was furred but not markedly so and his spleen was about an inch below the costal margin, but came down to about three inches on deep inspiration. His pulse was persistently below 100. A provisional diagnosis of enteric had been made, it was suggested that the course of the disease was being modified by inoculation, for he had received his first dose of TAB vaccine on the 12th and the second on the 22nd, and after each dose there was a sharp local reaction.

His temperature chart suggested malaria, but this diagnosis had been ruled out as highly improbable in the circumstances. I felt, however, that it was worth examining a blood smear and found a heavy malignant tertian infection; there were on an average of more than two rings per field and many erythrocytes had two rings or more in them. He was given quinine and made an uninterrupted recovery.

This finding led to the reconsideration of another case, a girl, aged 15, who had been in India seven years ago, but had not had malaria.

She first complained of fever on the 24th day of the voyage and the temperature rose sharply to 102° or 103° on the 26th, 27th and 28th, falling again to normal each evening. Her guardian who was a doctor gave her atabrin on the 27th after taking a blood smear; the temperature came down after two days, but from other observations a diagnosis of *B. coli* infection was made and the film was not examined. I did not see this patient, but I was asked to examine the blood film, which had been kept, and in the first field found two malignant tertian rings.

The ship's surgeon told me that two other patients, both Indians who had been in England some years and

had not had malaria during this period, had typical clinical attacks of malaria which responded to quinine, about this time.

In the first cases of these four the malaria was certainly acquired on board, the second almost certainly. All four cases were amongst 'tourist' class passengers who were accommodated in the stern of the ship and whose cabins were at a lower level than those of the first class passengers. At 'A' a certain number of country craft came alongside selling fruit and other things. Most of the trade was done with the 'tourist' passengers.

The patients were all four in different cabins and the cabins were some distance from one another so that it seems likely that (if they were all cases of malaria), more than one infected mosquito came on board.

That the infected mosquito(es) came on at 'A' seems almost certain. That they were on board before this can surely be ruled out, as they would scarcely have been lurking inactive since the ship touched at a malarious port about two months earlier, and nine days would be too short an incubation period to allow for their coming on at 'C', even if this were malarious and about this I have no information.

The malaria-carrying mosquitoes of 'A' appear to be *Anopheles gambiae* and *A. funestus*; I have not found any references to the range of these particular species.

As to how the mosquitoes came on board there are many possibilities. They may have been blown directly from the shore or they may have 'hopped' from ship to ship; they may have come in the oil lighter or the motor boats, or finally in the country boats with the fruit. Speculation on these points will not be very profitable, but it seems most likely that they were simply blown from the shore as there was a moderate wind off the land part of the time.

The incident does seem to suggest that the passengers and crews of ships lying even a mile from a malarious shore may become infected with malaria: the same remark will apply to yellow fever, and, as many ships will now be calling at 'A' and other West African ports on their way to India, the port health authorities in this country should consider whether the precautions they are taking are adequate to deal with this added danger, the addition being quantitative rather than qualitative.

I have been told that a similar incident occurred during, or shortly after, the last war and that Australian troops were infected with malaria whilst lying in the harbour at 'A'; I have been unable to find the reference to this incident.

Yours, etc.,

L. EVERARD NAPIER.

PS. 'A' is a port in West Africa.  
'B' and 'C' are islands off the west coast of Africa.

## Service Notes

### APPOINTMENTS AND TRANSFERS

#### To be D. D. M. S. of a Command

MAJOR-GENERAL A. C. MUNRO, K.H.P. Dated 6th May, 1940.

The Governor is pleased to appoint Lieutenant-Colonel K. S. Thakur, Civil Surgeon, 24-Parganas, to act as Surgeon-General with the Government of Bengal, during the absence, on leave, of Major-General P. S. Mills, C.I.E., with effect from the 10th September, 1940, or until further orders.

Lieutenant-Colonel G. Covell, C.I.E., and Major M. K. Afridi reverted from foreign service under the Indian Research Fund Association, with effect from the 1st April, 1940, and were retained in the posts of Director and Assistant Director, respectively, of the Malaria Institute of India under the control of the Central Government.

Major J. H. Boulton is transferred to the Semi-Effective List. Dated 2nd June, 1940.

Captain Shwe Zan, Civil Surgeon, Bhamo, on transfer, made over and Lieutenant-Colonel W. J. S. Ingram received charge of the duties of the Civil Surgeon, Bhamo, on the afternoon of the 5th August, 1940.

Captain C. C. Kapila, on reversion from Military, assumed charge of his duties as Officer on Special Duty at the Pathological Laboratory, Rangoon General Hospital, on the forenoon of the 20th August, 1940.

Captain F. W. Allinson, doing general duty at the Medical College Hospitals, Calcutta, is placed on general duty at the Presidency General Hospital, Calcutta, with effect from the 13th August, 1940.

The Secretary of State for India has appointed to the Civil Branch of the Indian Medical Service the following Officers of the Indian Medical Service, with effect from the dates stated against their names:—

#### Central Government

Captain I. J. Franklen-Evans. Dated 19th July, 1939.

Captain W. S. Morgan. Dated 17th August, 1939.

Captain C. L. Greening. Dated 19th December, 1939.

Captain L. S. F. Woodhead. Dated 21st December, 1939.

#### Madras

Captain P. L. O'Neill. Dated 25th August, 1939.

Captain T. E. Palmer, O.B.E. Dated 19th December, 1939.

Captain W. A. N. Marrow. Dated 24th November, 1939.

#### Bihar

Captain L. M. Kelly. Dated 26th December, 1939.

Lieutenants (on probation) L. Nendkeolyar and B. L. Kapoor are confirmed in their ranks. Dated 1st February, 1940.

#### INDIAN LAND FORCES. INDIAN MEDICAL SERVICE (Emergency Commissions)

##### To be Lieutenants (on probation)

Dated 10th June, 1940

Harcharan Lal Bhatia.

Dated 13th June, 1940

Saiyid Safdar Ali Khan.

Mohammad Abbas.

Mohindra Singh Boparai.

Tirath Ram Bargotra.

Ved Parkash.

Jitendra Nath Sen Gupta.

Dated 14th June, 1940

Santimoy Banerji.

Sailendra Kumar Sen.

Ahmad Husain.

Abdul Aziz Malik.

Bani Mohan Mukherjee.

Santosh Kumar Mukherjee.

Sunder Singh Sehgal.

Shiv Kumar.

Chaudhri Mohammad Ashraf Raza.

Krishnanand Jha.

Sheikh Mohammad Shafi.

Harkishan Singh.

Mohammad Ali.

Krishna Lal Banerjee.

Syed Haider Ali Gardezi.

Dated 15th June, 1940

Rattan Singh Sahi.

Anup Kumar Dutt.

Dattaram Wamanrao Khot.

Manakampat Madhavan Unni Nayar.

Mohammad Husain Alvi.

Ravi Varma Balachandran Tampi.

Ramchandra Dattatray Kamat.

Sukhdev Bhatia.

George Bartholomew Fernandes.

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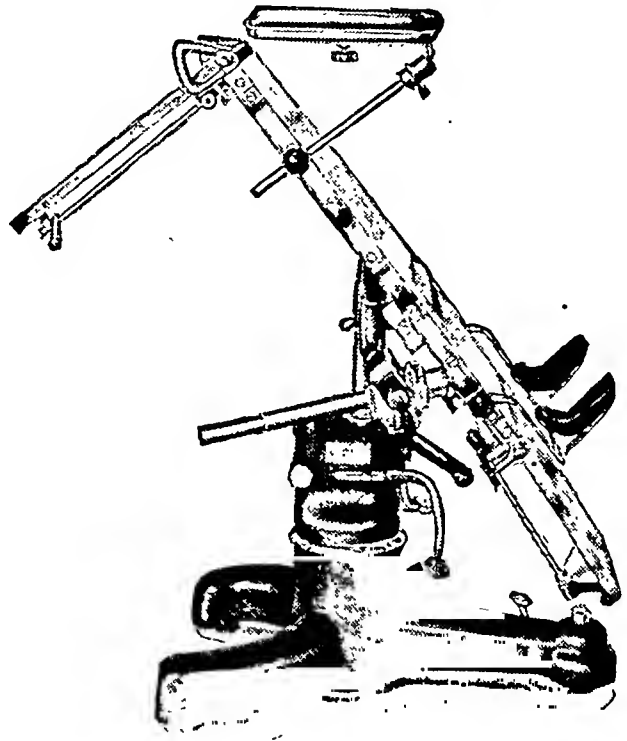
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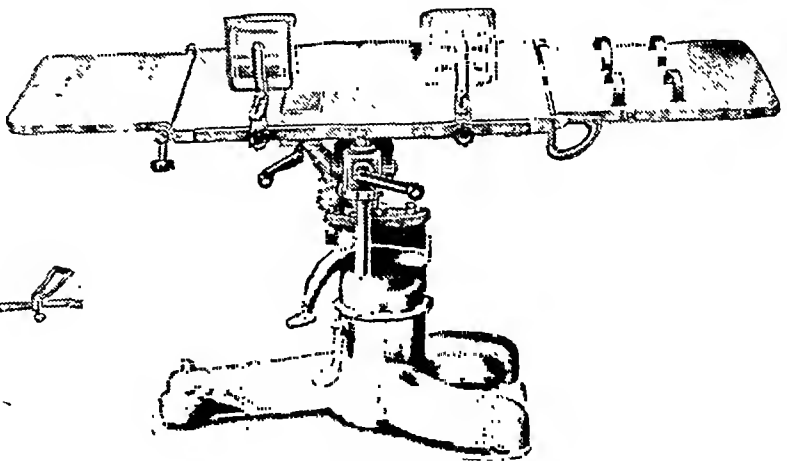
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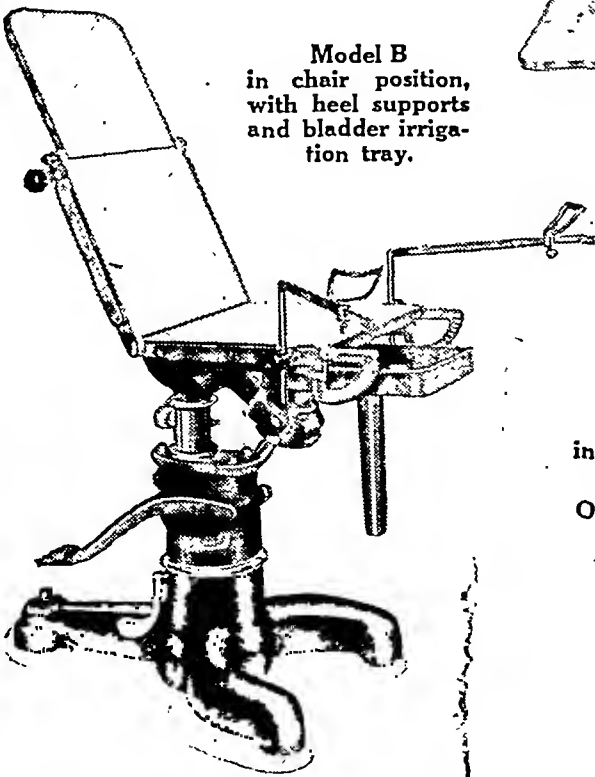
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Alagasingham Krishnan.  
Palamaneri Chaudra Sekar Srinivasan.  
Kesava Sivasankara Pillai.  
Chacko Wallapurackal Chacko.  
Hari Singh Kanwar.  
Mangudi Kailasa Tyagarajan.  
Kanwar Partap Singh.  
Syed Ali Aslam.

Dated 16th June, 1940

Venkatachalam Rajagopalan.  
Bertram William Lyall.  
Gostha Behari Bhattacharyya.

Dated 17th June, 1940

Kaivar Raghavendra Rao Rama Rao.  
Ouseph Francis.  
Subramanyam Ganapathiagraharam Rajagopal.  
Taravath Damodara Taravanar.

Dated 1st July, 1940

Rajindra Lal Mehta.  
Mohammad Nazir Khan.  
Manjeshwar Raghavendra Rao.  
Anil Kumar Mallik.  
Madhav Yashwant Alurkar.  
Suhrid Kumar Sen.  
Sham Singh Sekhon.  
Shiv Nath Narula.  
Bimalendu Ghosh.  
Amar Chand Bhataria.  
Mahabir Singh.  
Nawal Kishore Mehra.  
Trilochan Singh Parmar.  
Kali Kumar Das.  
Francis Chandra Das.  
Thomas Titus.  
Sushil Kumar Bhaumik.  
Satyes Chandra Ghosh.  
Ajit Kumar Sen Gupta.  
Anil Chandra Ray.  
Manakkampad Vasunny Nayar.  
Sitaramaiyer Ramalingam.  
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Narayan Chandra Bhowal.  
Nilakanta Sitaraman.  
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Suraj Deva Narayan Sinha.  
Ajit Kumar Das Gupta.  
Ganapathiagraharam Ananthasubramania Sundaram.  
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Nirmal Kumar Mitra.  
Kali Pada Roy Chowdhuri.  
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Daya Shanker Kaicker.  
Birendra Narain Mukherji.  
Navanitha Nayudu Santhanam.  
Manjeri Mavuppadi Rayaroth Veetil Anantan  
Nambiyar.  
Surjit Singh.

Dated 2nd July, 1940

Om Prakash.  
Niranjan Sen Gupta.

Dated 3rd July, 1940

Ali Khan Mohammad Mazhar.

Dated 4th July, 1940

Madhukar Mallannah Shrinagesh.  
Harris Arthur Satya Joseph.

Dated 5th July, 1940

Rameshchandra Bhaskar Sule.

Dated 15th July, 1940

Asita Lal Som.  
Arumana Raman Tampi.  
Ramakrishna Subramanian.  
Amar Prasad Ray.  
Madhao Ramchandra Tatwawadi.  
Ram Krishna Chakravarty.  
Rabindranath Ghose.  
Ganesh Chandra Sarkar.  
Gurmukh Singh.  
Muhammad Imamuddin.  
Gopal Vasudeo Chaphekar.  
Bharatsen Luxmanrao Somway.  
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Mehtar Singh.  
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Krishan Sarup Seth.  
Syed Abdul Wadud.  
Hari Dev Varma.  
Sardar Ahmad.  
Behram Boman Shah Choksi.  
Abdul Waheed.  
Swami Charan Prasad Sinha.  
Matety Sri Rama Rao.  
Nirmal Chandra Mukherjee.  
Ahmed Mohiuddin.  
Nihar Kumar Nag.  
Abdul Ahad Khan.  
Eswara Gangadhara Sastry.  
Manzur Ilahi.  
Saroj Kumar Das.  
Sudhir Chandra Bagchi.  
Dwarkanath Narainlal Rai.  
Sasanka Mohan De.  
Kallolickal Meeran Rowther Meeran Rowther.  
Hari Pada Bancrji.  
Arthur Benjamin Talibuddin.  
Shaikh Bazlay Rabbi.  
Charanjit Shah Singh.  
Parimal Dutt.

Dated 16th July, 1940

Arun Kumar Mukerji.  
Mohit Kumar Maitra.  
Santosh Kumar Bose.

Dated 17th July, 1940

Anil Kumar Das.

Dated 18th July, 1940

Eric Ronald Francis Rebello.  
Sib Das Basu.  
Kioithara Peter Joseph.  
Mampilly Augusty Paul.

#### LEAVE

The Governor is pleased to grant leave for the period from the 10th September to the 4th October, 1940, to Major-General P. S. Mills, *c.i.e.*, Surgeon-General with the Government of Bengal.

Major A. N. Chopra, Additional Assistant Director-General, Indian Medical Service, is granted leave for 1½ months, with effect from the 22nd August, 1940.

#### PROMOTIONS

*Lieutenant-Colonel to be Colonel*

H. Horan-Brown. Dated 30th July, 1940, with seniority from 31st July, 1936.

*Major to be Lieutenant-Colonel*

B. R. Tandon. Dated 25th August, 1940.

*Captains to be Majors*

E. H. Lossing. Dated 4th August, 1940.  
R. I. Reid. Dated 8th August, 1940.

#### RETIREMENT

Colonel F. F. S. Smith, *v.h.s.* Dated 30th July, 1940.

## Notes

### PYELECTAN

PYELECTAN is a preparation of the sodium salt of 3:5-di-iodo-4-pyridoxyl-N-methyl-2:6-dicarboxylic acid. This is the iodine compound which has achieved international reputation as a contrast medium for intravenous pyelography. The iodine content is firmly bound in organic combination, and is rapidly and completely excreted, unchanged, by the kidneys. Pyelectan is available in 20 c.c. ampoules, each containing in aqueous solution 15 grammes of the compound referred to. Literature and further details can be obtained from any branch of H. J. Foster and Company, Limited, India.

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pressure and contracting of pupils in glaucoma, and the aqueous solution is of considerable use in ozæna. To meet all these uses, Carbachol is issued as a 'Tabloid' product of 0.002 gm. for oral administration; as a 'Hypoloid' product of 0.25 gm. in 1 c.c. for subcutaneous or intramuscular injection; as 'Wellcome' (Ophthalmic) Solution of Carbachol, 0.75 per cent, with a convenient dropper; and as 'Vaporole' (Nasal) Solution, of 0.05 per cent.

### THE LOVIBOND COMPARATOR

THE Lovibond Comparator mentioned in the article 'Hæmatological Technique', Part V, by L. Everard Napier, F.R.C.P. (Lond.), and C. R. Das Gupta, M.B. (Cal.), D.T.M., on page 480 of the August number of the *Gazette* can be obtained from British Drug Houses, London, and stocks are now available at this company's depôts in India, Imperial Chemical House, Ballard Estate, Bombay, c/o H. S. Clark, Kent House, 33, Mission Row, Calcutta.

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## Original Articles

### A FURTHER REPORT ON THE TREATMENT OF SOME VIRUS DISEASES OF THE SKIN BY INJECTION OF SPECIFIC TISSUE FILTRATES

By L. M. GHOSH, M.B., D.T.M.

and

P. A. MAPLESTONE, D.S.O., D.Sc., M.B., B.S., D.T.M.

(From the Department of Dermatology and Medical Mycology, School of Tropical Medicine, Calcutta. Partly financed by the Indian Research Fund Association)

THE four skin diseases known, respectively, as molluscum contagiosum, infective warts, pityriasis rosea, and herpes zoster are now accepted by all dermatologists as being caused by filtrable viruses. The infectious nature of all of them has been proved by successful transmission of the diseases (in the case of herpes by production of varicella-like lesions in children) to healthy persons by injection of filtrates of tissue taken from the lesions.

Further evidence of the presence of a virus in herpes zoster has been advanced by Goodpasture and Teague (1923) who produced herpes-like lesions on the skin of guinea-pigs by inoculation with herpes blister fluid, and other workers claim to have caused an eruption on the pads of dog's feet by the same means. de Castro Teixeira (1936) produced typical pocks on developing eggs.

Maplestone and Panja (1939) described a regular train of symptoms leading to death, following the intracerebral inoculation of rabbits with both filtered and unfiltered molluscum material, and the brains of animals dying from this cause showed pyramidal cell degeneration. They were also successful in transmitting the infection through two series of healthy rabbits by inoculation with brain emulsion of animals dying from this artificial infection, but subsequent to this the virus apparently became attenuated because it only caused slight and transient symptoms on the third passage, and none of the rabbits died. Later they showed that the majority of persons who had recovered from an attack of this disease had specific antibodies in their blood, which could be demonstrated by means of an antigen prepared by a special technique from the preserved brains of the infected rabbits.

The same workers also obtained partial success by inoculating the chorio-allantois of developing eggs, according to the technique of Burnet (1936), but as in the case of the rabbit experiments, the virus seemed soon to lose its activity, as it always died out after three or four passages.

Preliminary reports on the results of treatment of these four diseases by means of injection

with filtrates made from material removed from active lesions and killed with 0.5 per cent carbolic acid, and later on with 0.1 per cent formalin, have already appeared.

Ghosh (1934) recorded the apparently successful treatment of six cases of molluscum contagiosum. Ghosh and Maplestone (1935) had similar favourable results in 12 cases of infective warts of the plane type, but failed in five cases of papillomatous warts. Maplestone and Dey (1937) reported 28 cases of pityriasis rosea treated on similar lines, in which the average duration of the disease was reduced by about half, and finally Maplestone and Ghosh (1938) reported 40 cases of herpes zoster in which the results were particularly striking because the severe and often persistent pain of this condition always disappeared, at the latest, after the second injection.

On account of these uniformly favourable results, we have made repeated attempts to cultivate all these viruses on the chorio-allantois of developing eggs in the hope that we would thus be able to establish the strains and have a reliable source of vaccine for treatment. But with the exception of the partial success with molluscum contagiosum, mentioned above, we have always failed. We have therefore had to rely on filtrates prepared directly from material taken from persons suffering with these various diseases. In this connection we have found that filtrates prepared from a number of cases and pooled are quite as good as a filtrate made from a particular case and used on that case only, following the principle of using an auto-vaccine.

Our investigation as to how long these filtrates maintain their activity as therapeutic agents is not yet complete, but we have kept them in an ice-chest for over a year and so far there seems to be no loss of potency. The method of preparation and the dosage of the various filtrates are essentially the same as that described in the preliminary reports. This method has now been standardized, and to enable those who have not access to our former papers, and who may be desirous of trying this form of treatment, we are giving a recapitulation of these particulars in an appendix to this paper.

#### *Molluscum contagiosum*

Duration of disease prior to treatment, months	Number of cases	CASES CURED		CASES NOT CURED	
		Number	Number of injections per case	Number	Number of injections per case
1 to 2	18	2	4	1	2
		4	5	1	8
		7	6	1	8
		1	7		3
		1	7		3
			7		*

\* See footnote on next page.

*Molluscum contagiosum—concl'd.*

Duration of disease prior to treatment, months	Number of cases	CASES CURED		CASES NOT CURED	
		Number	Number of injections per case	Number	Number of injections per case
2 to 3	8	1 2 2 1	3 5 6 7	1 1	3 4
3	5	2 2	5 7	1	7 2 3 } *
4	6	2 1 2 1	5 6 7 8		
5	7	4 2 1	6 7 6 5 } *		
6	9	1 1 2 1 1	4 5 6 4 5 3 6 } *	1 1 1	3 4 7
7, 8 and 9	8	3 2 2	5 6 8	1	7
12 or more	3	1 1	5 8	1	2
TOTAL	64	53	..	11	..

\* These patients ceased attending before a full course was completed and returned after an interval and treatment was resumed.

*Note.*—Only two of the uncured cases showed no response, so the failure of the others to be completely cured may be ascribed to their irregular attendance and the incompleteness of the courses of treatment. It is a coincidence that in the warts and pityriasis rosea series two cases were also not improved. In herpes all cases showed improvement.

*Infective warts (plane type)*

Duration of disease prior to treatment, months	Number of cases	CASES CURED		CASES NOT CURED	
		Number	Number of injections per case	Number	Number of injections per case
Less than 1	3	1 2	6 8		
1 to 2	7	2 2 1 1 1	6 7 8 10 6 6 } *		
2	8	1 3 1 1	6 8 9 10	1 1	4 6

\* See footnote to molluscum contagiosum table.

*Infective warts (plane type)—concl'd.*

Duration of disease prior to treatment, months	Number of cases	CASES CURED		CASES NOT CURED	
		Number	Number of injections per case	Number	Number of injections per case
3	12	2 2 4 1 1 1	5 7 8 9 10 5	1 1	8 4
4 and 5	7	2 3 1	5 7 8	1	4
6	16	3 2 3 2 2 1 3	4 6 7 8 9 10 8	2 1	6 9
1 to 10	4	1 1	11 8		
12 to 24	23	1 2 4 3 5 2 1	5 6 7 8 9 10 6 5 6 7 8 9 10 6 7 8 9 10 6 7 8 9 9	3 1 1	4 6 7
2×12 to 3×12	10	2 2 4 1 1 1 2 3 1	6 6 7 8 9 10 6 7 8 9 10 6 7 8 9 9		
3×12 to 8×12	12	1 2 3 1	6 7 8 9	1 1 1 1	6 7 8 9 6 } *
TOTAL	102	84	..	18	..

\* See footnote to molluscum contagiosum table.

In addition to the 102 cases recorded in the above table 20 cases with papillomatous warts, with histories of duration from 2 months to 9 years, were treated in the same way. Only two responded to treatment satisfactorily, one required nine and the other ten injections to effect a cure. Four others showed slight improvement and two of the remainder had courses of bismuth injections as well as the filtrate without any apparent effect.

As a control, 20 cases of plane warts and 31 of papillomatous warts were treated with bismuth injections and only one of each type was cured. These cases were not selected in any way.

The bismuth preparation used was 'Bismo-chin' which is made by a firm of Calcutta drug manufacturers and is much cheaper than imported preparations of bismuth suitable for injection. It has been used by us in a large number of cases of lupus erythematosus with satisfactory results so it is clearly an active preparation.

*Pityriasis rosea*

TABLE A

Duration of disease prior to treatment, days	Number of cases	CASES CURED		CASES NOT CURED	
		Number	Number of injections per case	Number	Number of injections per case
0 to 7 (A)	10	6 2 1 1	4 5 6 7		
8 to 14 (B)	17	1 3 6 6 1	2 3 4 5 6		
15 to 21 (C)	23	6 6 3 2 1	4 5 6 7 7	1 1 2 1	3 4 5 7
22 to 30 (D)	10	1 3 4 1 1	3 4 5 6 7		
1 × 30 to 2 × 30 (E)	20	1 7 3 1 1 1	3 4 5 6 7 8	4 1 1	4 5 6
2 × 30 to 3 × 30 (F)	10	2 3 2 1 1	4 5 6 7 8	1 1	5 8
3 × 30	5	1 1 1	5 6 6	2 1	5 6
4 × 30	1	1	5		
5 × 30	1	1	8		
TOTAL	97	81	..	16	..

\*See footnote to molluscum contagiosum table.

TABLE B

The average time in weeks taken to cure cases in each group from the beginning of treatment and from time of onset of the generalized rash

Group (see table A)	Average duration of treatment (in weeks)	Average time taken to effect a cure from onset of rash (in weeks)
A	2.3	3.2
B	2.3	3.8
C	2.52	4.5
D	2.27	5.3
E	2.4	6.1
F	3.0	11.5

(The cases not cured and those taking two courses of treatment have not been included in calculating the figures of this table.)

On account of the fact that pityriasis rosea is a self-limiting disease the duration of which is said to be from four to ten weeks, according to

different authorities, it is difficult to assess the value of this form of treatment. Nevertheless the figures given in table B, in our opinion, strongly suggest that this form of treatment shortens the duration of the attack in the majority of cases. It should be noted that the duration of the disease, and consequently the time taken to effect a cure after its onset, have been estimated from the time the generalized rash appeared, because evidence of the time that the herald patch is noted, if it is noted at all, is very unreliable.

*Herpes zoster*

Duration of disease prior to treatment, days	Number of cases	CASES CURED		CASES NOT CURED	
		Number	Number of injections per case	Number	Number of injections per case
1	2	1	2		
2	6	3	2		
3	10	3	3		
4	16	12	2		
5	10	3	4		
6	15	6	3	1	2
7	22	3	3	1	3
8	3	1	5	1	3
12	1	1	4		
15	1	1	4		
TOTAL	86	77	..	9	..

*Ophthalmic herpes*

1	1	1	4		
2	1	1	3		
3	4	3	3		
4	4	1	4		
5	2	3	4		
7	1	2	4		
9	1	1	4		
TOTAL	14	14			

*Post-herpetic neuralgia*

10	1	1	4		
12	1	1	4		
14	1			1	3
15	1			1	3
2 × 30	1			1	3
TOTAL	5	2	..	3	..

\*See footnote to molluscum contagiosum table.

In the total of 86 cases of herpes there were no complete failures. It will be noted in the 'not cured' column that only one of the nine cases took the maximum number of injections. They had evidently improved so much that they did not attend until completely cured.

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## APPENDIX

## DETAILS OF HOW TO PREPARE THE FILTRATES AND THE DOSAGE EMPLOYED

*Molluscum contagiosum, infective warts, and herpes zoster*

The lesions are cleaned, as far as possible, with a mixture of equal parts of ether and alcohol. They are snipped off with sharp scissors, curved on the flat, taking care that no normal skin is removed. The tissue is weighed by difference in a previously weighed sterile test-tube and placed in a sterile agate mortar with sterile pumice stone powder. It is energetically rubbed to make as fine an emulsion as possible and during the process sterile normal saline solution is slowly added until an amount of saline in proportion of 1 c.cm. to 1 mgm. of tissue has been used. The emulsified tissue is filtered through *Whatman's* No. 1 after which it is drawn through a *Whatman's* No. 1 candle under negative pressure. A quantity of normal saline containing commercial formalin in a strength of 2 per cent and equal in volume to the filtrate is mixed with it. This gives an emulsion in 1 per cent formalin-saline. It is tested for bacteriological sterility, and if free from contamination it is placed in a rubber-capped vaccine bottle and stored in an ice-chest for future use.

**Dosage.**—The initial dose is in all cases 0.1 c.cm. of the filtrate and in the case of warts and molluscum each successive dose is increased by 0.1 c.cm. until 1 c.cm. has been reached. The number of doses usually found necessary will be found in the tables in this paper. The interval between doses is three or four days (twice weekly). Where two courses have been given it means that the patient concerned ceased attending for a considerable time after the initial series of injections had been given, on account of considerable improvement but before cure was complete.

In the case of herpes the second dose is 0.2 c.cm. as in the other diseases but no further increase is made if more injections are needed. The injections are also given every second day instead of twice a week.

No local or general reaction has been produced even when larger doses than those recommended are employed, but as they did not appear to have any better effect there is no point in using them. In the case of herpes it is important to give no more than 0.1 c.cm. for the initial dose, because we have found if a larger dose is given it is liable to cause a severe exacerbation of symptoms.

(Continued at foot of next column)

## IMPROVED SIMPLE ENDO-TRACHEAL ANÆSTHETIC TECHNIQUE

By G. R. RAWLINGS, M.B., B.Ch. (Camb.), D.A. (Eng.)  
2/2, Harington Street, Calcutta

*Elimination of 'dead space'*

MANY anæsthetists, who have no suitable 'gas and oxygen' machine, employ endo-tracheal anæsthesia very successfully by using the simplest apparatus. Some system, such as a funnel covered with gauze and connected to the intra-tracheal tube, is frequently used to vaporize the anæsthetic agent on the principle of the original Hahn's cone. In operations around the face and neck it is often necessary to use a fairly long piece of tubing to connect the vaporizer with the intra-tracheal tube. On these occasions it frequently happens that the patient begins to breathe far more deeply than in open anæsthesia or when a carbon dioxide absorption technique is being used, and he continues to do so throughout the operation. By using a connecting tube of large bore there is little obstruction to respiration, but the respiratory depth is still much increased, so it is obvious that this is caused by a raised alveolar carbon dioxide concentration due to the 'dead space' in the tubing.

When nasal intubation is indicated one is sometimes compelled to use an endo-tracheal tube of relatively small bore. The patient

(Continued from previous column)

*Pityriasis rosca*

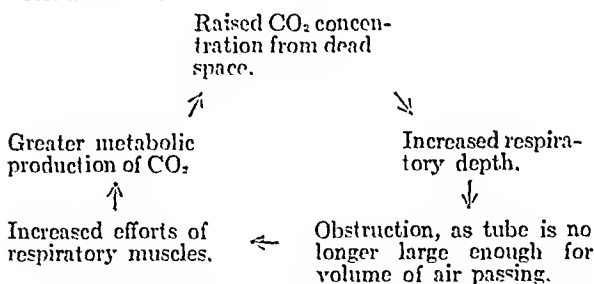
The virus of this disease gives the impression, both from its clinical manifestations and the few rather indefinite experimental records that are available, that it is of lower virulence than those which cause the other three diseases. We accordingly use a much more concentrated filtrate, and on account of the lesions being practically flush with the skin surface the method of collecting the material is of necessity slightly different.

A freshly-erupted spot 1 to 1½ cm. in diameter is selected and thoroughly cleaned with ether-alcohol. It is anæsthetized by injection beneath it of a little 2 per cent novocaine. A circular incision is made with a sharp knife. Care is taken that the depth of the incision is exactly the thickness of the skin, and it encircles the inflamed spot just inside the border so that no normal skin is included. The portion of skin outlined by the incision is dissected off carefully so that the whole skin is removed but no subcutaneous fat is taken with it. The wound is closed with one or two horse-hair sutures and dressed. The portion of skin is weighed by difference in a test-tube and shaken up with some normal saline to remove as much blood as possible. The saline is poured off and the skin transferred to an agate mortar where it is treated in the same way as already described, except that the saline is added in proportion of 1 c.cm. to 10 mgm. of tissue. After filtration an equal quantity of 2 per cent formalin in normal saline is added and if found sterile it is placed in a rubber-capped vaccine bottle and stored in the usual way.

**Dosage.**—Injections are given twice weekly beginning with 0.1 c.cm. and increasing each successive dose by 0.1 c.cm. up to 0.5 c.cm., after which no further increase is made. If by the time six injections have been given there are no distinct signs of improvement it is not worth continuing further. Many cases, however, do not need more than four or five injections to effect a cure.



breathes quite comfortably through this, but, when the apparatus has been connected for some minutes, the breathing begins to increase in depth until the respiratory efforts finally become very exaggerated and remain so throughout the anæsthesia. This is the result of a vicious circle.



To prevent this rise in the carbon dioxide concentration I have had made a simple unidirectional valve. This is inserted close to the intra-tracheal tube and thus prevents re-breathing into the connecting tube. By this means practically all the 'dead space' is eliminated, therefore making a closer approach to the normal physiological conditions of respiration.

This valve consists of two pieces of brass tubing  $1\frac{1}{4}$  inches in diameter, which fit together by a screw thread. A segment is cut from the circumference of one, and a brass plate is soldered across the resulting hole. This plate has a rectangular hole in it approximately  $1 \times \frac{1}{2}$  an inch. Another plate, in which is a hole of suitable shape, is soldered across the threaded (male) end of the other piece of tube. The shape of these holes is not important as long as they are sufficiently large to cause no obstruction to respiration. Smaller pieces of serrated brass tube, for the attachment of rubber tubing, are fixed to each end of the complete unit. Pieces of thin rubber sheet are partly stuck to the plates so as to cover the holes. These pieces of rubber act as flutter valves. I have found that 'Durofix' is a good adhesive for sticking the rubber to the brass. The metal parts can be made by any competent mechanic for a very small sum.

Figures 1 and 2 will make the construction and function clear. The rubber flap A opens on inspiration and shuts on expiration, whereas the flap B works in the opposite phase, with the

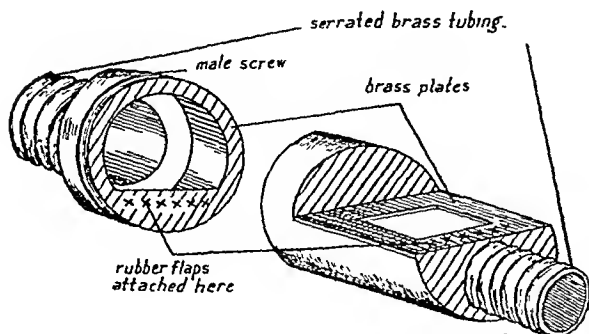


Fig. 1.—Unidirectional valve.

result that no re-breathing can take place into the connecting tube. These rubber flaps should be as thin as possible, to offer the minimum obstruction to respiration. On the other hand if too thin they will be driven through the holes.

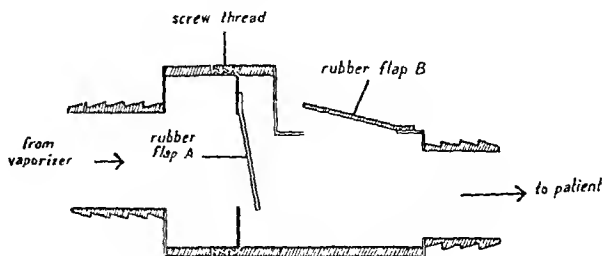


Fig. 2.—Valve in section.

I have found that much quieter breathing results from using this valve, and thereby a smoother anæsthesia is usually obtained. When indicated, a smaller endo-tracheal tube may be used satisfactorily as the conditions causing the vicious circle, referred to above, no longer are present. It will be seen that one obvious advantage of using this valve is economy, since vaporization of the anæsthetic agent only takes place on inspiration.

A wire cage, fitted over the expiratory valve, is useful in preventing the valve from being obstructed by towels, etc.

#### *An efficient ether vaporizer*

A very efficient ether vaporizer can be made for a few annas in a short time by any one capable of using a soldering iron. The essential components are a large and a small tin, a piece of brass tube, a small tap, copper mesh, and some stout copper wire. Actually, 1-pound and 5-ounce Squibb's ether tins were used, but obviously any tins of similar shape will serve. The construction of this apparatus can be seen from figures 3 and 4. A small tap is soldered into a hole made in the bottom of the smaller tin, which is to act as the ether reservoir. A convenient and easily obtained tap is of the type used in saline infusion apparatus. It is essential that it should work smoothly and be capable of delivering a slow steady drip. A hole is made in the side of the lower part of the large tin. A piece of brass tube with a diameter not less than  $\frac{3}{4}$  inch and about  $1\frac{1}{2}$  inches long is soldered into this hole. The large tin is packed loosely with copper mesh. This is readily obtained by unravelling a copper saucepan scourer. The smaller tin is now fixed above the large one with stout copper wire, so that the tap is immediately over the centre hole in the top of the large tin.

The third tin shown at the bottom of the apparatus is not essential but, when filled with hot water, it prevents condensation owing to the rapid cooling effect of the evaporating ether. Also, the added weight makes a firm base for the apparatus.

The upper tin is filled with ether, and the side hole in the large tin is connected to the intra-tracheal tube. By adjusting the tap, a steady drip of ether falls on to the copper mesh, and is there evaporated by the passage of the patient's respirations. A hypodermic needle, pushed through the cork, maintains atmospheric pressure in the upper tin, and thereby prevents an uneven flow of ether.



Fig. 3.—Ether vaporizer.

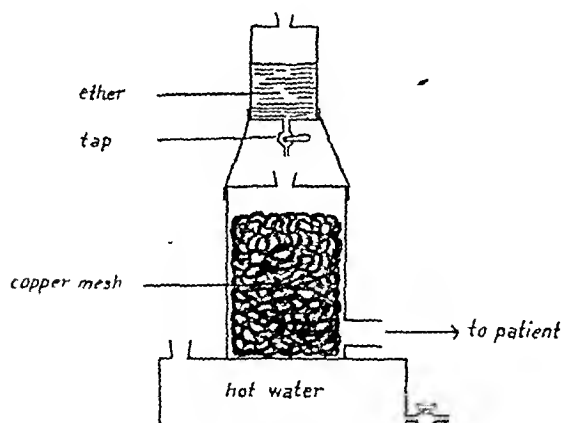


Fig. 4.—Vaporizer in section.

I have found that, when combined with the valve described above, an extremely smooth anaesthesia can be achieved with this vaporizer. The patient is offered a steady concentration of ether, which can be rapidly and evenly increased, when necessary. Owing to this unvarying concentration of ether, a very light level of anaesthesia can be maintained for a considerable time without coughing or gagging setting in. The longest single anaesthesia, for which I have used this apparatus, was of three and a half hours'

(Continued at foot of next column)

## FURTHER CASES OF TYPHUS FEVER IN BOMBAY CITY

By T. B. PATEL, B.Sc., M.B., B.S., B.Hy., D.P.H.  
(Infectious Diseases Hospital, Arthur Road, Bombay)

PATEL (1940) reported some cases of typhus fever among the patients admitted to the above hospital from the city as suspected cases of the typhoid group; since then, we have continued our investigations and found eight more cases of a similar nature; these are detailed below.

In this series, one case is an imported one, while the rest occurred among the population of the city; each of them gave a history of residence in Bombay for the last two years or more and none of them had been out of Bombay for at least one year prior to his present illness.

From a survey of these cases, together with the cases previously reported, it is noticed that (i) all except one occurred in males, (ii) most of them occurred in different parts of the city, with the exception of two cases (no. 4271 and no. 4317) which occurred within the same mill compound, (iii) most of the cases occurred in the lower middle class and working class population, and (iv) they were distributed among all communities, Hindus, Muslims and Christians in that order of preponderance. The two cases which occurred in one mill compound were from different houses separated from each other by a distance of more than a hundred yards; one of these was a watchman and the other a clerk. The one imported case (no. 4140) was a wandering beggar who came to Bombay from Nagpur four days prior to the onset of the disease. It must be mentioned that only a very small percentage of the cases suspected of the typhoid group of infection seek admission into our hospitals in this city; and, in consequence, there is reason to believe that a number of cases of typhus fever escape detection.

Furthermore, typhus fever has all along been looked upon in this city as a disease of extremely rare occurrence and, in consequence, no special attempt has hitherto been made to look for it. From the Annual Reports of the Executive Health Officer of this city, it will be observed that one case of typhus fever has been hitherto reported in the year 1917 and also one each in

(Continued from previous column)

duration. About 10 ounces of ether were used, and the patient, who was a large man, suffered no post-anaesthetic vomiting, nor any other distress whatsoever. The apparatus is very economical, doubly so of course when combined with the valve. It may be used with a rubber face mask or with a well-fitting intra-pharyngeal airway. If ether alone is used, the apparatus is not satisfactory for the induction of anaesthesia. Used with a face mask and the valve, it is excellent for induction with chloroform owing to the steady concentration of vapour given.

1932, 1933 and 1937. With a view to discovering the ætiology of this disease, we made a searching examination for lice of each patient admitted to the hospital, and closely questioned him as to any history of insect bites; from these inquiries it would appear that both the louse and the tick could in all probability be excluded

of plague in this city, and it seems to us that there is ample justification to regard the rat flea as the vector of typhus also in this city. How far this is true needs further experimental investigation. All the cases so far investigated do not present any of the classical signs and symptoms which are regarded as characteristic

TABLE I

Reg. no.	Admitted on	Day of disease on which admitted	Sex	Age	Caste	Occupation	Locality	Clinical features	REMARKS
4271	10-12-39	8th	M.	35	H.	Watchman.	Parel	No rash; temperature up to 102°F., came to normal on 11th day of disease by lysis; drowsiness and headache on admission.	
4317	25-12-39	11th	M.	20	H.	Clerk	Parel	Toxæmia marked; temperature up to 102°F., came to normal on 16th day of disease; drowsiness; blood-shot eyes; severe headache and general body-ache which were a marked feature the first two days after admission.	
4140	9-12-39	10th	M.	60	M.	Mendicant.	Bhendy Bazar R. Side.	Toxæmia moderate; joint pains; blood-shot eyes; temperature came to normal on 12th day of disease by lysis; bronchitic signs in the chest.	Imported from Nagpur.
832	24-1-40	8th	M.	30	H.	Labourer	Delisle Road.	Complained of headache on admission; slow pulse; temperature ranged up to 101°F. and came to normal on 13th day by lysis.	
1038	4-2-40	9th	M.	42	H.	Clerk	Khetwadi	Signs of slight bronchitis; continuous fever rising to 103°F. for 11 days; emperature came to normal on 13th day of disease by lysis. Complained of headache and back-ache.	
1425	22-3-40	10th	M.	34	Ch.	Working in a bakery.	Byculla	Signs of bronchitis; continuous fever rising to 101°F., came to normal on 16th day of disease by lysis.	
1685	2-4-40	8th	M.	40	Ch.	Vendor of piece cloth.	Mazagaon	Continuous fever for 13 days; temperature rising to 103°F.; drowsiness; severe pains in all the joints and general headache; toxæmia marked; temperature came to normal on 14th day by lysis; patient complained of deafness for a fortnight after the temperature came to normal.	
1883	10-4-40	4th	F.	18	M.	Nil	Bhendy Bazar.	High temperature of 103.5°F. on admission; continued to be high with slight remissions; marked drowsiness; delirium; blood-shot eyes; severe headache, back-ache and joint pains; marked toxæmia; died on the 7th day of disease. Hyperpyrexia (106.5°F.) before death; no rash; no rigidity of neck, Kernig's sign negative; pupils reacted to light; lungs clear; spleen not palpable.	

as the causative agent. All the cases which we have so far examined have given a positive Weil-Felix reaction with X19 antigen supplied by the laboratory at Kasauli. The rat flea has been incriminated in such cases from investigations carried out in other parts of India. Rat infestation is quite a common feature in most of the houses in Bombay; they are especially abundant where the poorer classes dwell. We are all familiar with the history of the spread

of this disease, except that most of them complained of severe joint pains and general body-ache along with an elevated temperature, and that the temperature came down to normal between the 11th and the 16th days of the disease, usually by lysis, in some cases there was a marked conjunctival injection. Most of the cases were admitted to the hospital after the 7th day of the onset of fever, hence we had no opportunity of examining them at an earlier

stage. The diagnosis had to be made mainly on the positive serological tests, after excluding the typhoid group of infection. We have summarized the history and clinical features of these

3. We believe that the disease in this city is conveyed by rat fleas, an opinion based on analogy with plague, pending further experimental investigations.

TABLE II  
*Serological reactions*

No.	Reg. no.	Date	X19	X2	XK	Widal tests
1	4271	22-12-39	1 : 320	1 : 40	— ve	— ve
		26-12-39	1 : 1,280	1 : 40	— ve	— ve
		1-1-40	1 : 2,560	1 : 80	— ve	
2	4317	26-12-39	1 : 320	— ve	— ve	— ve
		30-12-39	1 : 2,560	1 : 80	— ve	— ve
3	4140	11-12-39	1 : 160	— ve	— ve	— ve
		14-12-39	1 : 320	— ve	— ve	— ve
		18-12-39	1 : 640	— ve	— ve	
4	832	27-2-40	1 : 640	1 : 80	— ve	— ve
		3-3-40	1 : 1,280	1 : 640	— ve	— ve
5	1038	7-3-40	1 : 80	— ve	— ve	— ve
		12-3-40	1 : 640	1 : 40	1 : 20	— ve
6	1425	23-3-40	1 : 160	— ve	— ve	— ve
		31-3-40	1 : 320	— ve	— ve	— ve
		6-4-40	1 : 640	1 : 80	— ve	
		9-4-40	1 : 320	1 : 20	— ve	
7	1685	5-4-40	1 : 640	1 : 80	1 : 20	— ve
		9-4-40	1 : 1,280	1 : 40	— ve	— ve
		27-4-40	1 : 160	1 : 20	— ve	
8	1883	12-4-40	1 : 80	— ve	— ve	— ve

cases in table I and the results of agglutination tests in table II. It must be noted that there was one death (no. 1883) in this series; this was a young girl sent in as a case of typhoid fever. On bacteriological examination, both the blood culture and the Widal test were negative; the Weil-Felix reaction gave an agglutination of 1 : 80 with the X19 antigen on the sixth day of the disease, according to the history given by the patient. Examination of blood smears for malarial parasites, a routine procedure with all cases admitted, was also negative. A differential count gave the following results: polymorphonuclears, 51 per cent; lymphocytes, 43 per cent; eosinophils, 1 per cent; and large mononuclears, 5 per cent. The temperature rose to 106.5°F. before death; and we could detect no complications in the lungs; this death was in all probability due to the intense toxæmia. There was no history of any other case of fever in the family.

#### *Summary*

1. Within the last ten months we have found 15 cases of typhus fever (based on the Weil-Felix reaction) among the cases admitted as suspected 'typhoid group' of infection.

2. In view of the prevailing attitude that typhus fever is a very rare and uncommon disease in Bombay city, a certain number of cases of typhus fever go undetected.

We take this opportunity of thanking Dr. B. P. B. Naidu who drew our attention to the possibility of typhus infection in some of our earlier cases and to his co-operation in this work and to Dr. P. T. Patel, the superintendent of the hospital, for his permission to record these notes.

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#### A SHORT NOTE ON THE MASS ANTHELMINTIC TREATMENT BY OIL OF CHENOPODIUM AND TETRACHLOROETHYLENE\*

By D. C. MAJUMDER, L.M.P. (Assam)  
*Daimukhea Tea Estate, Doom Dooma P. O.,  
Upper Assam*

In tea gardens in Assam, hookworm infection is one of the greatest problems that confronts the medical department especially in the rainy season when the full efficiency of the labour force is most needed. An examination carried out by a helminthic expert on a batch of coolies selected at random in this district gave 100 per

\* Read at a meeting of the Doom Dooma and Associated Tea Companies' Medical Society held on 27th April, 1940.

TABLE I  
Showing the hæmoglobin index by Tallqvist's scale from the year 1938 to 1940

Hæmoglobin	80 per cent			75 per cent			70 per cent			65 per cent			60 per cent			55 per cent			50 per cent			45 per cent			40 per cent			35 per cent			Total		
	38	39	40	38	39	40	38	39	40	38	39	40	38	39	40	38	39	40	38	39	40	38	39	40	38	39	40	38	39	40			
Year ..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..			
BALIJAN																																	
Lines:—																																	
Bilaspur ..	..	..	..	..	..	1	..	..	5	..	4	35	95	76	173	67	78	19	34	16	5	6	5	..	..	..	..	..	..	202	179	238	
No. 6 ..	..	..	1	..	..	1	..	..	31	3	3	117	216	249	299	158	169	38	46	34	21	6	5	7	..	..	..	1	..	430	460	515	
No. 12 ..	..	..	..	..	..	1	..	..	38	4	2	162	244	319	321	171	195	29	79	24	4	25	4	1	7	2	..	..	1	530	546	557	
TOTAL ..	..	..	1	..	..	3	..	..	74	7	9	314	553	644	793	396	442	86	159	74	30	37	14	8	7	2	..	1	..	1,162	1,185	1,310	
BURRA BHEEL																																	
Lines:—																																	
SL and HL	..	..	..	..	..	..	..	..	9	..	..	18	..	40	115	..	52	22	..	26	6	..	6	1	..	..	..	..	..	..	124	171	
New ..	..	..	..	..	..	..	..	..	19	..	5	87	..	123	147	..	115	23	..	25	3	..	10	2	..	..	..	..	..	..	278	231	
Old ..	..	..	..	..	..	..	..	..	27	..	8	154	..	145	252	..	71	31	..	146	14	..	15	2	..	1	1	..	1	..	387	481	
T.L. ..	..	..	..	..	..	..	..	..	8	..	1	30	..	96	123	..	89	34	..	24	11	..	7	3	..	..	..	..	..	217	209		
No. 2 ..	..	..	..	..	..	..	..	..	2	..	3	45	..	132	223	..	106	102	..	38	15	..	18	2	..	1	..	1	..	298	390		
TOTAL ..	..	..	..	..	..	..	..	..	65	..	17	334	..	536	860	..	433	212	..	259	49	..	56	10	..	1	2	..	2	..	1,304	1,532	
GRAND TOTAL	..	..	1	..	..	3	..	..	139	7	26	648	555	1,180	1,653	396	875	298	159	333	79	37	70	18	7	3	2	1	2	1	1,162	2,489	2,842
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cent infection. As a result of this infection a large number of the population get foot sores and anæmia which cause great disability. This entails dislocation of work, which means an economic loss to the estate. It was therefore decided in 1938 to give a mass treatment for hookworm infection by oil of chenopodium and tetrachlorethylene as recommended by Chopra (1936) and Maplestone and Mukerji (1937). Hare and Dutta (1939) have found these drugs to be of great value in this respect.

The treatment was given to practically the whole population of this estate. This estate consists of two big sections, viz (1) Baliyan and (2) Burra Bheel. In 1938 only Baliyan was given the treatment and the other side was kept as a control. Finding the results encouraging, as shown in tables I and II, both sections were treated in 1939 and 1940.

#### *Management and details of the treatment*

(1) The people were informed the previous day that they should (a) not take alcoholic drinks for twenty-four hours, (b) should come to the hospital the next morning at 7 a.m., and (c) have no food that morning.

(2) All being assembled, a thorough enquiry was made as to whether they had abstained from alcoholic drinks for the previous twenty-four hours and whether they had had food that morning. Anybody found not taking these precautions was disallowed treatment for that day.

(3) All adults and children from 6 months upwards were given the treatment.

(4) Dosage used was oil of chenopodium 1 c.cm., tetrachlorethylene 3 c.cm., and saturated solution of magnesium sulphate 2 oz. for an adult of average health. Proportionately reduced dosages were administered to younger and less robust people. These drugs were freshly mixed in a number of one-pound bottles and thoroughly shaken up before administration. The well-shaken emulsion took a milky appearance. Precaution was taken to wash the medicine glass between each patient with warm water, for fear of overdosage.

(5) The hæmoglobin index of every individual was recorded by Tallqvist's scale.

(6) They were kept under strict observation of the medical staff all the time they were at hospital. All were made to pass their stools in the hospital septic tank latrine and on no account were allowed to go into the neighbouring tea.

(7) After the bowels had moved properly a spoon diet was given to all of them consisting of boiled sago and sugar. They were all kept at hospital up to 5 p.m. when a light meal consisting of rice and dāl was given to them and then they were allowed to go to the lines with the instruction, not to take any alcoholic drinks for at least that night.

(8) An average of 236 people were treated daily with the exception of Saturday, Sunday and Monday, the days when coolies usually do most of their drinking.

(9) They were given *hazira* (wages) for the day of treatment.

#### *Complication of treatment*

There were no complications during the treatment except some cases, who in spite of warnings came to hospital with a full stomach, to which they did not admit. After taking the medicine they vomited badly, which frightened some of them. One of these cases fainted as a result of vomiting and had to be put to bed. He recovered after a while without any treatment.

#### *Cost of treatment (excluding hazira)*

Two thousand eight hundred and forty-two people were treated in 1940; medicine cost Rs. 105 and diet Rs. 175 bringing the total cost to Rs. 280; thus the average cost per head was approximately As. 0-1-7. In my opinion, this expenditure was fully justified when one considers the encouraging results and improvements as shown in tables I and II. After treatment the low-grade-anæmia cases had also to remain for a shorter period on the 'anæmic list', as shown in table III.

TABLE II

*Showing the percentages of anæmia cases before and after treatment*

BALIJAN									BURRA BHEEL								
Before treatment			After treatment						Before treatment			After treatment					
1938			1939			1940			1939			1940					
Number treated	Number of anæmics	Per cent	Number treated	Number of anæmics	Per cent	Number treated	Number of anæmics	Per cent	Number treated	Number of anæmics	Per cent	Number treated	Number of anæmics	Per cent	Number treated	Number of anæmics	Per cent
1,162	214	18.41	1,185	90	7.51	1,310	39	2.97	1,304	318	24.39	1,532	61	3.98			



TABLE III

*Showing the duration of treatment for anæmia before and after anthelmintic treatment*

Average days on anæmic list before anthelmintic treatment	Average days on the anæmic list after anthelmintic treatment	Number of days gained
13	10	3

TABLE IV

*Showing the incidence of foot sore cases before and after anthelmintic treatment*

BEFORE TREATMENT	AFTER TREATMENT	
Average of three years from 1935 to 1937	1938	1939
95	72	20

### Discussion

The result of mass hookworm treatment has proved to be a success by the decrease of low grade anæmia and appreciable rise in hæmoglobin index. By low grade anæmia is meant those whose index is 50 per cent and below. If such an improvement could be maintained in future, low grade anæmia will gradually be a thing of the past. It will be seen from tables II and III that the anæmic percentage of the whole population has been considerably reduced and the labourers on the anæmic list could be discharged three days earlier. This is not only a saving of medical expenditure but also an economy to the estate, as more labourers can be put to a full day's work, thereby reducing the cost of production. With the improvement of their blood condition, the general health and efficiency of the labour force will be much improved. It will also increase their powers of resistance, enabling them to withstand acute diseases, such as pneumonia, more effectively. This treatment has also considerably diminished the foot sore incidence of the estate as is shown in table IV. This has reduced the number of out-door patients as well as prevented the wastage of labour at a most important time. With the increase of hæmoglobin and good health it is hoped that in the near future it will have a salutary effect upon the incidence of maternal mortality, still births and infant mortality in general. The treatment was much appreciated by the labour force. Many of them hold that this treatment, 'julap' as they call it, has done them immense good.

(Continued at foot of next column)

## SHORT-TERM FEVERS IN LUCKNOW

By H. SAHAI

*Professor of Medicine, Lucknow University, and Physician, King George's Hospital, Lucknow*

and

S. C. BANERJEE

EVERY year with marked regularity, Lucknow is visited by an acute specific fever of short duration, which hitherto has been in a sporadic form, but this year has appeared in epidemic form with differences in toxicity, severity, and manifestations. The first indication of this outbreak was a sudden increase in the hospital attendance for fever. With the exception of a couple of cases of short-term fever which occurred earlier, the epidemic of short fevers began in July, thus coinciding with the breaking of the monsoon, and rapidly commenced to wane in November, no case being admitted to the hospital in December. Cases occurred among people of all classes and in both sexes, but especially in young adults. We followed a number of these cases, as many of the students of the Lucknow University, including medical college students and nurses, were admitted at the onset of the attack.

(Continued from previous column)

### Summary and conclusions

- (1) A mass hookworm treatment was carried out safely and successfully with oil of chenopodium and tetrachlorethylene.
- (2) The incidence of anæmia and foot sore has considerably diminished as a result of this treatment.
- (3) The general health and physical well-being of the labour force has much improved.
- (4) There were no serious complications arising out of the treatment.
- (5) The cost per head of medicine and feeding was approximately As. 0-1-7.

### Acknowledgments

I am greatly indebted to my chief, Dr. H. Flack, for his valuable advice while carrying out this experiment. My thanks are also due to Mr. J. Batterbury, Manager, Daimukhea T. E., for his keen interest, support and encouragement in all medical affairs. I have also to thank my compounder staff for their loyal co-operation in this undertaking.

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 Maplestone, P. A., and Mukerji, A. K. (1937). *Ibid.*, Vol. LXXII, p. 650.

The cases were characterized by the presence of joint pains, prostration, cough, and irritation of the throat. Some of them have been returned as cases of influenza, but the majority as 'pyrexia of unknown origin', and some as sandfly fever, dengue fever group, and febricula. These fevers are probably all alike in their ætiology and symptomatology. The ultimate diagnosis, when they are grouped in this list, depends mostly on the course the disease takes as regards time, type of fever, rash, intensity of muscular and joint pains, blood picture, and variation in pulse. All these fevers are common in the United Provinces though they are more prevalent in epidemic and pandemic forms in Bengal, Bombay, Madras and other places situated near the coast.

The main characters of the febrile attacks were as follows: The onset was usually sudden, with a feeling of chilliness not amounting to actual rigor. Pain in the eyes, deep at the back of the eyeball or a superficial burning or pricking sensation in the conjunctivæ was most characteristic, and a great diagnostic help during the first two or three days. The conjunctivæ were often swollen, reddened and injected. There were aching pains in the back and lower limbs but they were not so marked as in textbook descriptions of 'break bone' fever. The symptoms reached the height of their severity at the end of 48 to 72 hours and then diminished as the temperature fell. The temperature came down to normal on the 3rd, 5th, 7th, or 9th day with general improvement in the condition of the patient. The face lost its flushed appearance, pink eyes disappeared, the retro-ocular pain was forgotten and the patient decidedly improved. The patients now clamoured for food. In a large number of cases the convalescence was uninterrupted, but in some it was noticeable that after an apyrexia of 48 to 72 hours, the temperature rose a second time, with a recurrence of all the old symptoms, though in a milder form. On the 8th day the temperature fell again to normal and stayed there. Thus we were definitely dealing with two distinct classes of pyrexia, one with a single pyrexial period, the other with an initial pyrexia of 48 to 72 hours' duration followed by 24 to 48 hours' fall in temperature to the level of a little above normal, and then a secondary rise which lasted for 24 hours (saddle-back type). Only three cases showed rash, a generalized macular rash which lasted 3 to 4 days. The tongue was usually clean, a clinical sign of importance in differentiating from typhoid fever. Seven per cent of the cases had bowel disturbances in the form of loose and frequent motions; the rest had constipation. Five cases had nausea and vomiting during the fever. Abdominal pain was marked in several cases, and some of them started with this symptom, together with marked toxæmia simulating typhoid fever. The pulse rate was not invariably on the slow side as reported by various observers. The rise in pulse rate was

proportionate to the rise in temperature in 43 per cent of the cases. Swelling of glands was not observed. Insomnia was troublesome in a few cases. Delirium was present at the height of fever in four cases. There were no complications seen in the cases analysed. We have had no mortality in spite of alarming symptoms in some instances.

*Investigations.*—In all cases in which blood examination was carried out malarial parasites were not detected, even after repeated examination of blood smears.

The total leucocyte count was normal or raised in 68 per cent of cases, the rest had leucopenia. In some cases, as low a total count as 4,400 per c.mm. was observed. There was no definite variation in the differential leucocyte count. There was in some cases relative increase of lymphocytes and not a decrease, as reported by some observers in this disease.

Blood culture, taken in agar medium from the patient when the temperature was at its height, proved sterile after 48 hours' incubation.

The Widal reaction against *B. typhosus*, *B. paratyphosus A*, *B. paratyphosus B*, *B. paratyphosus C*, *B. faecalis alkaligenes*, and *B. suis-pestifer* was negative in twenty-five cases in which it was done.

Stool culture was negative for non-lactose fermenters and streptococci.

Throat swabs were taken from all the cases and culture proved negative for *Streptococcus hæmolyticus*.

*Animal experiment.*—Eight c.cm. of blood from the ante-cubital vein of a patient on the 2nd day of fever, mixed with 2 c.cm. of sterile 3.8 per cent sodium citrate solution, was injected into the peritoneal cavity of a guinea-pig. Also, an equal quantity of blood from a normal individual mixed with sodium citrate solution of the above strength was injected into the peritoneal cavity of another guinea-pig of approximately the same size and weight. Rectal temperature was taken morning and evening at specified hours and a careful watch was kept for any reactions that followed. Rectal temperature of another healthy guinea-pig was also recorded. This was to serve as a basis on which to judge any fluctuations in temperature following the injection. The control animal had a reactionary rise in temperature following the injection which lasted 24 hours after which the temperature came down to normal and remained there, and the animal was active again. The experimental animal had a rise in temperature to a higher level, which dropped by crisis to rise again for a second and third time. The temperature chart closely resembled that of the patient. The animal was very listless and refused food till the temperature had finally settled. This animal inoculation experiment indicates that the blood of a patient suffering from short-term fever is infective in the first few

days, but what the nature of this infection is we do not know.

### Illustrative cases

We have very carefully investigated 119 cases admitted to the King George's Hospital. They can be grouped under the following heads:—

(i) Common type ..	70 cases
(ii) Short type ..	18 "
(iii) Long type ..	14 "
(iv) Abdominal type ..	6 "
(v) Toxic type ..	9 "
(vi) Relapsing type ..	2 "

In all the cases recorded below the following investigations were done with uniformly negative results.

Blood film—Negative for malarial parasite.

Blood culture—Sterile after 48 hours' incubation.

Stool culture—Negative for non-lactose-fermenters.

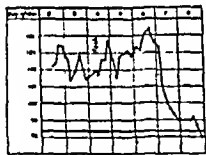
Throat swab culture—Negative for *Streptococcus haemolyticus*.

Widal against salmonella group—Negative.

**Common type.**—Case 1. Female, age 18 years, was admitted on the 2nd day of fever. The onset was abrupt. The patient complained of headache (frontal), pain in limbs, and nausea. Nothing abnormal was detected on physical examination.

Rash appeared on the 4th day. It was macular and generalized. There was relative bradycardia. The temperature came down to normal by crisis on the 7th day.

CHART 1

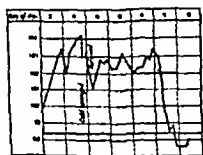


No complications occurred. The appearance simulated enteric fever with frontal headache and slight abdominal discomfort, but proved to be one of short-term fever.

**Case 2.**—Male, age 20 years, was admitted on the 2nd day of fever. The onset was abrupt. The patient complained of headache (occipital) and pain in eyeballs. There was abdominal pain but no bowel irregularity. Nothing abnormal was detected on physical examination.

No rash appeared.

CHART 2



Rise in pulse rate was proportionate to rise in temperature. The temperature came down to normal by crisis.

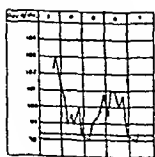
Total leucocyte count—10,960 per c.mm.

Differential count—polymorphonuclears 72 per cent; lymphocytes 22 per cent; eosinophiles 2 per cent and large mononuclears 3 per cent.

No complications occurred.

Abdominal pain was a marked feature in this case.

CHART 3



**Case 3.**—Male, age 18 years, was admitted on the 3rd day of fever. The onset was abrupt. The patient complained of headache and pain in the eyes. On physical examination, throat was found congested and the spleen enlarged three fingers.

No rash appeared. There was relative bradycardia. The temperature came down to normal by lysis.

Total leucocyte count—8,400 per c.mm.

Differential count—polymorphonuclears 62 per cent; lymphocytes 34 per cent; eosinophiles 1 per cent and large mononuclears 4 per cent.

No complications occurred. The spleen was enlarged in this case probably due to previous attacks of malarial fever.

**Case 4.**—Male, age 24 years, was admitted on the 2nd day of fever. The onset was abrupt. The patient complained of headache and pain behind the eyeballs. Physical examination showed that the spleen was just palpable.

No rash appeared. Rise in pulse rate was proportionate to rise in temperature. The temperature was typically saddle-back type.

Total leucocyte count—8,400 per c.mm.

Differential count—polymorphonuclears 60 per cent; leucocytes 38 per cent and large mononuclears 2 per cent.

No complications occurred.

**Short type.**—Male, age 20 years, was admitted on the 1st day of fever. The onset was abrupt, accompanied by a chilly sensation. The patient complained of headache and pain in limbs. Nothing was found on physical examination.

No rash appeared. There was relative bradycardia. The temperature came down to normal by crisis.

Total leucocyte count—9,600 per c.mm.

Differential count—polymorphonuclears 72 per cent; lymphocytes 22 per cent; eosinophiles 2 per cent and large mononuclears 4 per cent.

No complications occurred.

**Long type.**—Male, age 18 years, was admitted on the 6th day of fever. The onset was abrupt, accompanied by a chill (not rigor), headache and vomiting. The patient complained of headache and pain in the chest. There was not much pain in his body, but he suffered from considerable restlessness. Physical examination detected congestion of throat and eyes.

No rash appeared. There was relative bradycardia. The temperature was of a saddle-back type.

Total leucocyte count—8,200 per c.mm.

Differential count—polymorphonuclears 80 per cent; lymphocytes 18 per cent and eosinophiles 2 per cent.

No complications occurred.

**Abdominal type.**—Male, age 20 years, was admitted on the 1st day of fever. The onset was abrupt. The patient complained of headache (parietal), pain in the joints and eyeballs. There was generalized abdominal pain but no bowel irregularity. On physical examination nothing abnormal was detected.

No rash appeared. Rise in pulse rate was proportionate to rise in temperature. The temperature came down to normal by crisis.

Total leucocyte count—12,240 per c.mm.

Differential count—polymorphonuclears 70 per cent; lymphocytes 27 per cent and large mononuclears 3 per cent.

No complications occurred. Abdominal pain was a marked feature in this case, and persisted throughout the course of illness.

CHART 4

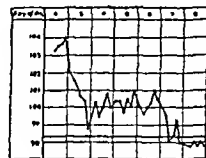


CHART 5

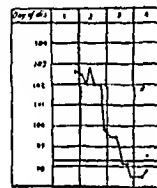


CHART 6

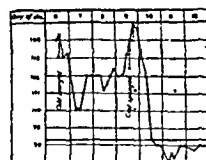


CHART 7



**Toxic type.**—Male, age 20 years, was admitted on the 2nd day of fever. The onset was gradual. The patient complained of pain in abdomen (epigastrium), chest, and the whole body. On physical examination, he looked very toxic (2nd day). The tongue was coated and dry. There were sordes on teeth and lips.

No rash appeared. There was relative bradycardia.

**Differential count**—polymorphonuclears 46 per cent; lymphocytes 49 per cent; eosinophiles 2 per cent and large mononuclears 3 per cent.

No complications occurred. The patient was toxic throughout the course of illness.

**Relapsing type.**—Female, age 9 years, was admitted on the 1st October, 1939, on the 6th day of fever. The onset was gradual. The patient complained of headache in the beginning, pain in abdomen and body. No abnormal signs were detected on physical examination. The temperature came down to normal, by crisis, on the 8th day, and she left the hospital cured. She was re-admitted on the 15th of October with a relapse of fever (see charts 8 and 9).

Patient re-admitted on the 15th October, 1939. She had been afebrile for six days after the first attack.

No rash appeared.

CHART 8

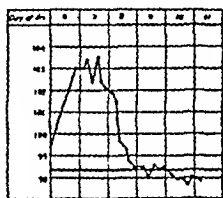
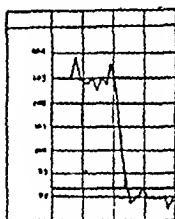


CHART 9



We had only two cases of this type which were quite free from fever and other symptoms, for about six days. This may be due to the relapsing nature of this group of fevers, which is most often seen in typical dengue fever epidemics, or it may be due to the predisposition caused by early attacks of this fever during an epidemic. It seems certain that one attack does not give rise to any prolonged immunity, as it is a common experience that people may suffer from 'short fevers' repeatedly year after year.

### Conclusions

The febrile attack labelled seven-day fever, sand-fly fever, and pyrexia of unknown origin appear to be one and the same disease.

Although similarities may be detected in the course of fever, the condition is distinct from dengue, at least symptomatically, by less severe pain, less abrupt fall of temperature, and less marked relapses.

Relative bradycardia is not a constant feature of this condition.

Normal or slightly raised white blood count is more common than leucopenia.

The rash, primary or secondary (except in three cases) as commonly seen in dengue, was absent.

Lung complications and signs being absent, the condition could not be confused with influenza.

The actual cause of the disease is still unknown.

[The clinical description does not appear to exclude either dengue or sandfly fever as the diagnosis in these cases.—Eaton, I. M. (7)]

## DEMONSTRATION OF AN ALLERGEN IN FILARIASIS AND ITS UTILIZATION IN THERAPEUTICS

By R. K. GOYAL, M.B., D.Sc., Ph.D., M.R.C.P.

and

S. SUNDAR RAO

(From the Filariasis Inquiry under the I. R. F. A., School of Tropical Medicine, Calcutta)

ALTHOUGH it is now almost universally accepted that lymphangitis is in some way connected with infection with the filarial worms, *Wuchereria bancrofti* and *W. malayi*, the exact mechanism by which the exacerbations and remissions occur in these patients is by no means clear. Anderson and his colleagues (1924), as a result of careful and detailed investigation of this problem in British Guiana, came to the conclusion that 'infestation by *Filaria bancrofti*, per se, produces no symptoms; all the pathological manifestations associated with filariasis are due to secondary infection with pyogenic organisms'. This was the view held by previous workers. Wise and Minnett (1913) investigated several cases of abdominal filariasis in British Guiana in 1911 and reported the finding of streptococci in all these cases. The importance of streptococcal infections was dwelt upon by Rose (1915, 1919) and by Grace and Grace (1931). On the other hand, O'Connor and Hulse (1932) were of opinion that advanced pathological changes in filarial infection could be solely due to the parasites without the secondary bacterial infection. The work reported herein was carried out with a view to finding the rôle of bacteria in the causation of lymphangitis.

Fifty cases of filariasis in the out-patient department of the School of Tropical Medicine, mostly in the early stages of the infection, were examined for the presence of a secondary bacterial infection. The material was obtained with sterile precautions from the affected areas (glands, scrotum, leg) and cultured both aerobically and anaerobically. The results were entirely negative. Blood taken from febrile cases and cultured, similarly gave negative results. The superficial dermal lesions were not taken into consideration. In one case of a small superficial abscess in the leg, hæmolytic streptococci were isolated. The febrile attacks in these cases of filariasis thus appeared to be due, not to a bacterial factor but to the parasite alone. The periodic nature of attacks of lymphangitis suggests that these exacerbations are due to the presence of a toxin giving rise to allergic manifestations. In fact, Acton and Rao (1929, 1930) had drawn attention to the presence of a toxin in the uterine fluid of the gravid adult worm. It was therefore decided to investigate this question further. In view of the great difficulty of obtaining material from filarial cysts, the hydrocele fluid was used for investigating the presence of a toxin.

### Technique

Antisera were raised in rabbits by intraperitoneal injections at bi-weekly intervals of 10 to 30 c.cm. of hydrocele fluid containing microfilariae. Flocculation tests were put up with samples of hydrocele fluid against immune rabbit sera; the cerebro-spinal fluid was used as a control for the antigen. Serial dilutions of the immune serum were prepared in 0.25 per cent formol saline, equal amounts (0.25 c.cm. to 0.5 c.cm.) of hydrocele fluid were added and the mixtures incubated at 37°C. The reaction was visible in about 4 hours and took 48 to 72 hours to be completed. In the case of a weakly positive reaction a faint turbidity was perceptible, a granular precipitate was visible in a moderate reaction, and definite floccules were found in strongly positive cases.

In general, the low dilutions of the serum gave rise to flocculation and higher dilutions produced either a precipitate or a faint turbidity. The titre of the serum was low, i.e., 1/16 to 1/32 in cases receiving 6 to 7 injections, but the titre rose to 1/128 to 1/256 after 14 consecutive injections. Out of 152 cases examined 106 flocculated from 24 per cent to the full titre of the serum, whilst 46 cases gave positive reactions varying from 2 per cent to 12 per cent of the titre. The cerebro-spinal fluid obtained from cases of meningococcal meningitis flocculated up to 12 per cent of the titre. Flocculation up to 12 per cent of the titre was thus due to the formation of non-specific antibodies and was taken to mean absence of a specific antigen, positive results were considered to be obtained when the flocculation occurred from 24 per cent to the full titre of the serum.

The toxin content of the hydrocele fluid was determined at intervals of some weeks in a few cases, marked variations were noted in certain cases, the titre ranged from 1/32 to 1/128. The *dirofilaria* antigen failed to flocculate even with the undiluted anti-filaria sera, showing thus the antigenic dissimilarity of the two worms. The globulin fraction of the hydrocele fluid flocculated as well with the antiserum as with the whole antigen; this strongly suggested the association of the toxin with the globulin fraction of the hydrocele fluid. Fluids obtained from a case of lymph scrotum and from a blister on the leg of a case of lymphangitis gave positive flocculation reactions. Similar results were obtained with fluids aspirated from filarial cysts. The hydrocele fluid, diluted even in 1 in 4, had its activity markedly reduced, whereas the fluid from cysts, diluted even in 1 in 10, gave strongly positive reactions *in vitro*; this observation shows the maximal concentration of the toxin near the worm and one can conclude that the worm is the source of the toxin.

Heating the filaria antigen at 55°C. for one hour reduced its potency from 1/128 to 1/8. When 1/2 dilution of the antigen was exposed to 100°C. for 15 minutes, the potency was

markedly reduced. In view of the thermostability of the toxin, it should be stored at a low temperature.

The presence or absence of microfilariae did not affect the flocculation titre in any way. Quite a number of fluids free from microfilariae gave positive reactions with high dilutions of the serum. The amount of the antigen had also no close relationship with the clinical condition of the patient. Marked thickening of the scrotal skin was sometimes associated with a low toxin content of the hydrocele fluid.

The complement-fixation test also revealed the presence of the antibody in the immune rabbit serum. No antibody was demonstrable by the flocculation or complement-fixation tests in the sera of eight human beings suffering from filariasis.

The toxicity of the fluid for mice was determined; 5 c.cm. of a good flocculating antigen killed two mice in 48 hours, smaller doses had no effect. Mice which had received a smaller dose some days previously resisted the lethal dose of 5 c.cm.

An intradermal injection of 0.1 c.cm. of the hydrocele fluid into normal rabbits and guinea-pigs produced a negligible local reaction, but a well-defined papule was produced in immunized rabbits in early stages of immunization; they behaved like normal animals later on; this observation shows that the development of a state of hypersensitiveness is followed by immunity. Intradermal injections of  $L_3$ -candle filtrates of high flocculating hydrocele fluids produced a definite papule with flushing of the surrounding skin in normal persons and filarial cases. A 1/10 dilution did not produce any appreciable reaction in normal people, but a majority of early filarial cases gave a marked allergic reaction. The most marked reaction consisted of (a) marked local swelling with surrounding erythema attaining dimensions of 6 cm. by 10 cm., (b) a febrile reaction—the temperature rising to 100°F. or 101°F., and (c) definite exacerbation of the local lesion in the way of increase of swelling, pain and flushing. The reaction generally started 4 to 8 hours after the injection and lasted for 12 to 48 hours. After the subsidence of the symptoms, the patients noticed an amelioration in their condition. The observation was utilized in the treatment of cases. The early cases suffering from periodic febrile attacks and increase of swelling showed marked improvement in the majority of cases. Some of the early cases and chronic cases in general did not give any reaction but showed an improvement in their signs and symptoms.

### Treatment

Out of the 76 cases followed carefully, 20 were acute cases and 56 chronic cases. All the 20 acute cases were either cured for the time being or showed a marked improvement. Out of the 56 chronic cases, 51 decidedly improved and five were unaffected by treatment. These five were cases of either orchitis or hydrocele.



In view of the ease and frequency of reinfection, it is not possible to say if a curative agent of the early condition has been discovered, but a marked amelioration of the symptoms in early stages can be brought about in most of the patients by this treatment.

#### *Abstract of cases of special interest*

**Case 812/40.**—A Hindu girl, aged 18 years, admitted on 26th April, 1940, for elephantiasis, of both legs and left hand and forearm, of six years' duration with history of acute lymphangitis at irregular intervals of two weeks or a month or two affecting only one limb at a time, with marked general and local signs and symptoms. Patient was put on antigen treatment on 26th April, commencing with 0.2 c.cm. gradually increased to 2 c.cm. twice weekly; a total of 14.4 c.cm. was given. Patient reported after about three months that she has been free from lymphangitis since the treatment began and the swellings of the limbs considerably reduced with marked improvement in general health.

**Case 737/40.**—Hindu male, aged 59, medical practitioner, admitted on 12th April, 1940, for elephantiasis of the scrotum with history of acute lymphangitis every full moon and new moon during the first two years and at irregular intervals subsequently, temperature ranging from 104° to 105°F. each time with rigor, swelling, redness and pain in scrotum, the acute exacerbation lasting 48 to 72 hours. Filarial antigen treatment given—a total of six doses (6.7 c.cm.). Has remained free from acute symptoms for about three months and feels well.

**Case 230/40.**—Hindu male, aged 29, admitted for chyluria of five years' duration on 12th April, 1940. Chyluria has appeared and disappeared previously at intervals without treatment. Previous treatment for the condition with vaccines, soamin and antimony compounds has had no effect. Blood and chylous urine—positive for microfilariae. Filarial antigen treatment given from 12th April to 23rd July, total 44.2 c.cm. Result—Urine cleared after 1.7 c.cm. of antigen treatment and remained so for 25 days. Relapse. Result of subsequent treatment has been indifferent.

**Case 822/40.**—Hindu male, aged 24, admitted on 26th April, 1940, for epididymo-orchitis and hydrocele (R); two years' duration; hydrocele tapped on 26th April. Filarial antigen treatment given (total 14.5 c.cm.). Hydrocele has not filled up again and patient feels better generally.

**Case 261/40.**—Hindu male, aged 29, admitted on 9th February, 1940, for elephantiasis of the right leg of 14 years' duration. Acute lymphangitis off and on, the temperature often rising to 106°F. with shivering, headache, pain all over the body and extreme thirst, such attacks recurring sometimes once a week, or once in three or six months. Filarial antigen treatment given since 9th February. Total amount given up to 23rd July—41.2 c.cm. Patient has been gradually improving in health, free from fever and the leg reduced to half the original size.

**Case 655/39.**—Mohammedan male, aged 30, admitted into the Carmichael Hospital for Tropical Diseases on 20th July, 1939, for urticaria of three years' duration. He was suffering from filarial lymphangitis of the scrotum and hydrocele. The urticarial eruptions appeared at intervals to begin with, and latterly were more severe and appeared daily. Other investigation, having proved negative, the patient was referred to us for filarial investigation and treatment. Test for filarial allergy—strongly positive; flocculation test with hydrocele fluid—moderately positive. Patient was treated with filarial antigen and the urticarial attacks ceased altogether.

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## OPHTHALMOPLEGIA IN PERIOSTITIS OF THE SPHENOIDAL FISSURE

By P. K. GUHA, M.B., M.R.C.S. (Eng.), D.O.M.S. (Lond.)  
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THE involvement of nerves during their course through bony canals due to the inflammation of the periosteal lining is well exemplified by Bell's (facial) palsy. What actually happens is a pressure effect by swollen periosteum and the inflammatory exudate, and thus a temporary interference with their function. That there is no permanent damage is proved by the complete recovery of function sooner or later in all such cases. A group of symptoms that may arise as a result of almost similar periostitis of the sphenoidal fissure and the resulting pressure involvement of the nerves passing through the fissure has been lately realized and such cases have been brought to light, occasionally. But on a search into the available English literature\* on the subject we failed to find reports of any such cases within the last few years. The pathology of the condition closely simulates that of Bell's palsy, as far as the mechanism of the nerve involvement is concerned.

To understand the clinical syndrome of these cases, a short description of the anatomy of the sphenoidal fissure will be of assistance.

#### *Anatomy*

The sphenoidal (superior orbital) fissure lies between the roof and the lateral wall of the orbit. The fissure is composed of a narrow outer limb and a wider medial limb. The outer limb is closed by dura mater and nothing passes through it. All the structures pass through the wider medial limb. The structures passing through the medial part are related to the annulus of Zinn. Above the annulus pass the lacrymal, frontal and the trochlear nerves, the superior ophthalmic vein and the recurrent lacrymal

\*The condition is described in Price's *Textbook of the Practice of Medicine*.—EDITOR, I. M. G.

(Continued from previous column)

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artery. Passing within the annulus are the superior division of the oculomotor nerve, the nasociliary and the sympathetic root of the ciliary ganglion, the inferior division of the oculomotor and the abducens, and sometimes the inferior ophthalmic vein, in this order from above downwards. The abducens nerve passes from below the inferior division of the third to lie lateral to and between the two divisions. Below the annulus, nothing passes as a rule; rarely the inferior ophthalmic vein takes this course.

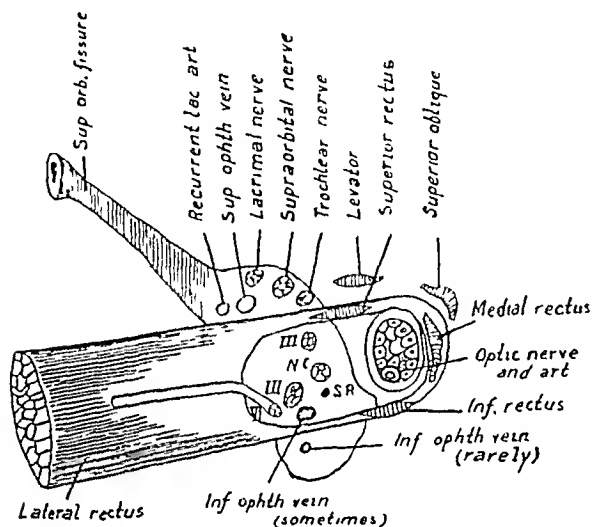


Diagram of the structures passing through the sphenoidal fissure.

III—Upper and lower divisions of the 3rd nerve.

N.C.—Nasociliary.

VI—6th nerve.

(From 'The Anatomy of the Eye and the Orbit'—Eugene Wolff.)

### *Ætiology and symptomatology*

Periostitis of the sphenoidal fissure forms a part of orbital periostitis. It occurs in all ages from puberty onwards. The periostitis may result as an extension of infection from the nose and the accessory sinuses. Syphilis also may be a contributory factor. Besides these cases there occurs a group of cases, in which no definite ætiological factor can be ascertained. They are usually thought to be due to rheumatic infection. It may be pointed out that gummatus affections of the orbit are extremely rare. The incidence is from 1 per cent to 2 per cent of all cases of syphilis of the eye and 0.013 per cent of all diseases of the eye as opposed to the so-called rheumatic group of cases which is gradually being found to be comparatively more common.

The chief feature of this condition is interference with the function of the structures passing through the sphenoidal fissure. The structures mainly involved are the nerves passing through the fissure. The onset is usually sudden, with pain and slight proptosis and there is slight tenderness on pressing the globe backwards. These signs are soon followed by involvement of the ocular nerves, the sixth nerve

is usually affected first; gradually the fourth nerve, the first division of the fifth, the third and the second divisions of the fifth nerves are involved in the order mentioned. The patient may complain of diplopia to start with. In a fully developed case, there is complete ptosis, with slight proptosis. The pupil is dilated and light reflex is either absent or sluggish. The eyeball is practically immobile owing to ophthalmoplegia. In spite of ocular palsy the patient at this stage does not complain of diplopia because of ptosis. There is some degree of anæsthesia in the distribution of the ophthalmic division of the trigeminal nerve, i.e., on the forehead of the affected side. The condition usually subsides within a period of six to eight weeks. In some cases it may be prolonged for a few months. Complete recovery is usually the rule.

Before a case is diagnosed as sphenoidal periostitis one should exclude the possibility of orbital tumours and metastatic carcinoma of the orbit, and a skiagram of the orbit and the accessory sinuses should be taken as a routine procedure, for the sake of completeness of investigation.

Treatment is chiefly symptomatic. Local application of warmth, mercury and salicylates orally, and analgesics for pain may be given. In cases where spirochætal infection is the ætiological factor, antisyphilitic treatment should be advised. To start with, mercury and iodides are given orally, followed by arsenic and bismuth injections.

### *Illustrative case*

A middle-aged male complained of pain in the right eye, headache, a sensation of fullness and throbbing inside the right eye. The onset of this group of symptoms was fairly sudden. About two or three days before these complaints, he had occasionally double vision on looking to the right. When first seen, he had slight proptosis and paresis of the right external rectus, the right pupil was comparatively larger and showed a less brisk light reflex compared to that of the left side. When next seen about a week later, he showed complete ptosis, all the muscles of the eyeball were paralysed, the eyeball remaining practically immobile, the pupil was dilated and light reflex absent. The eyeball was tender. There was slight anæsthesia over the right side of the forehead. The vision in the right eye was 5/6 partial with approximate glasses and the fundus oculi was normal.

There was nothing noteworthy in the past history. The general development of the patient was fair. Blood pressure was S/D = 140/100 mm. of Hg. Urine showed no abnormality. Blood sugar was 100 mgm. per 100 c.c.m. of whole blood. Hæmoglobin was 80 per cent, red blood cells—4,160,000 per c.c.m., white blood cells—5,600 per c.c.m., polymorphonuclears—70 per cent, lymphocytes—23 per cent, large mononuclears—1 per cent, eosinophils—6 per cent. Coagulation time—three minutes.

Wassermann reaction of the blood was strongly positive. Radiology of the skull and the orbit and sinuses revealed no abnormality.

The patient was advised local application of warmth, rest to the eyes, and was given iodides and salicylates and later on iodides and mercury orally. The eye condition returned to normal within a period of eight weeks. He was given a course of arsenic and bismuth later on.

(Continued at foot of next page)

## HEALTH CONDITIONS AND HEALTH WORK IN A FAMINE AREA

By C. M. NICOL, M.A., M.D., D.P.H.

LIEUTENANT-COLONEL, I.M.S.

Director of Public Health, Punjab

IN 1939, as in the preceding year, rainfall was lower than normal in the Punjab, and in certain areas of Hissar, Rohtak, and Gurgaon districts rains failed entirely.

Hissar district has suffered from famine repeatedly during the past 50 years or more, but within living memory famine has never been so intense or so prolonged as it has been during the latest visitation.

Scarcity of food was being felt in Hissar by the middle of 1938, and famine was officially declared in December of that year; in Rohtak and Gurgaon districts, test works were established in December 1938 and February 1939, respectively.

An idea of the extent to which these districts were affected may be gathered from the number of individuals who were attending relief works

(Continued from previous page)

This case presents all the typical features of sphenoidal periostitis. The negative radiological evidence, rapid onset and complete clearing of all symptoms definitely exclude the possibility of any tumour in the orbit, either primary or metastatic. Williamson-Noble (1926) brought to notice a rare group of cases, diagnosed as 'inflammatory pseudo-tumour' of the orbital tissue causing 'proptosis, limitation of movements, increase in bulk of the orbital tissue and possibly swelling of the orbit'. Actual palsy of the oculomotor nerves has not been mentioned. The onset of this condition is very slow. The reported case does not seem to belong to this group. It is very difficult to state whether the case is one of so-called 'rheumatic' or of syphilitic infection. The condition improved completely within eight weeks with iodides and mercury orally, which may be taken as a therapeutic test for syphilitic infection. But the usual course of such periostitis in the rheumatic group of cases is about eight to ten weeks. The positive Wassermann reaction therefore may be a matter of coincidence, the case belonging to the so-called 'rheumatic' group of cases and syphilis may not be the actual ætiological factor.

### Summary

(1) A case of sphenoidal periostitis with ophthalmoplegia is reported.

(2) The case illustrates all the classical features of the condition.

(3) The ætiology and the symptomatology have been discussed.

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organized by Government by the end of March 1939 :—

	Hissar	Rohtak	Gurgaon
Total number of workers including dependants.	202,389	29,738	10,051
Total population; 1931 census	899,479	805,621	740,163
Percentage attendance ..	22.5	3.7	1.3

### The earlier effects of famine

In February 1939, the diets and state of nutrition of 90 families in the famine areas, consisting of 529 individuals, were investigated by Dr. M. M. Khan, nutrition officer, Punjab public health department. The figures relating to diets and state of nutrition quoted below are taken from data collected by him.

The families were classified as follows :—

(1) Those whose members were engaged on relief works, lived in their villages, and came daily to work;

(2) Workers who had come from a distance and had arranged accommodation for themselves near the works; and

(3) Villagers not engaged on relief works.

Table I shows the average daily diet of 30 families in each of these three groups.

Table II gives the approximate nutritive values of the average diets detailed in table I.

The calorie values of the diets may be regarded as satisfactory, taking into consideration the comparatively light character of the manual labour on which the workers were engaged.

The most striking feature of the diets is their qualitative defects. Animal fat in any shape or form is either absent or present in negligible amount. Milk also is either absent or present in very small amount, and then only as skimmed milk. Green vegetables are entirely absent. The comparative absence from the diets of milk, ghee and vegetables means that the diets are very low in vitamin content: vitamin 'A' is present in quite inadequate quantity and vitamins 'C' and 'D' are absent altogether. Of the mineral salts calcium is very definitely deficient. Animal protein also is present in very small amount.

In short, the diets if adequate in quantity are extremely ill-balanced and contain a preponderance of carbohydrate material.

The state of nutrition of 279 workers and 144 non-workers, living on the diets detailed in table I, was estimated by physical examination: 82 per cent of the former were considered definitely subnormal physically and 50 per cent of the latter. The relatively better physical condition of non-workers appears significant: these individuals were not only consuming more milk and ghee than the workers, but also were exerting themselves to a much lesser extent.

Of 423 persons examined, 6 per cent complained of night-blindness, 25 per cent showed

TABLE I  
Average daily diet of families

Class of individuals	Number of families	Number of individuals	FOODSTUFFS EATEN									NUMBER OF FAMILIES HAVING				
			Cereals	Pulses	Vegetables	Fat	Skimmed milk	Sugar	Condi-ments		Milk		Green vegetables	Ghee or other animal fat		
									Salt	Chillies	Number	Average amount daily.		Number	Average amount daily.	
1. Relief workers living in their villages.	30	188	876	31	2	N	66	..	17	2	8	240	0	1	2	
2. Non-relief workers living in their villages.	30	190	782	79	18	2	256	..	19	3	18	432	0	5	13	
3. Workers from a distance living at the works.	30	151	799	12	7	..	..	..	10	5	0	..	0	0	..	

The quantities of foodstuffs are stated in grammes per adult male consumption unit.

The outstanding characteristic of these diets is the complete absence of green vegetables, the complete absence of animal fat in group 3 and the negligible (N) quantity of animal fat partaken of in the other two groups. Milk is also absent in group 3 diets and very small amounts of milk are included in the diets of the other two groups.

The 'average' daily diet was estimated as follows:—

The quantities of foodstuffs consumed by each family per day were accurately weighed and recorded before cooking, on two successive days. The total of these quantities divided by 60 gives the average diet per family per day in each group.

TABLE II  
Nutritive values of diets

Class of individuals	Number of families	Number of individuals	Total calories	PROTEIN		FAT		Carbo- hydrate	MINERAL SALTS			VITAMINS		
				Total	Of animal origin	Total	Of animal origin		Calcium	Phosphorus	Iron	(In inter- national units)		
												'A'	'B'	'C'
1. Relief workers living in their villages.	30	188	3,243	99	2	22	..	656	0.4	2.5	48	1,217	1,128	..
2. Non-relief workers ..	30	190	3,142	117	10	22	2	606	0.8	2.8	49	1,436	1,424	..
3. Labourers from a distance living at the works.	30	151	2,854	93	..	18	..	575	0.4	2.5	47	1,098	1,509	..
Minimum requirements for an adult male.	..	..	2,800 to 3,000	100	20	45 to 60	22 to 30	500	0.6	1.0	30	3,000	300	30

Quantities of protein, fat, carbohydrate and salts are stated in grammes. Iron and vitamin C are in milligrammes.

the dry roughened condition of the skin described as phrynodema, and 65 per cent smokiness of the sclera—signs of vitamin-A deficiency: 1 per cent showed signs of active rickets and 6 per cent of old-standing rickets, indicating vitamin-D deficiency.

These were the findings, notwithstanding the fact that a scale of relief pay higher than that authorized by the Punjab Famine Code had been introduced. It seemed clear that there was a danger of food deficiency conditions developing in more acute form and in increasing

numbers, and also that other diseases might be expected to prove much more serious in a community in which vitality had been lowered by qualitative and quantitative food shortage.

Arrangements were made for fresh vegetables to be made available to relief workers to as great an extent as limited supplies made possible, and individuals reporting sick at dispensaries with definite signs of A and D vitamin deficiency were treated with cod-liver oil.

Intensive general measures of hygiene were maintained including chlorination of water-supplies, the sanitation of camp areas and lines of work, the protection of 194,539 individuals against cholera by anti-cholera inoculation, and systematic vaccination throughout the district: 246,500 vaccinations were carried out.

#### *The later effects of food scarcity*

With the onset of the cold weather greater physiological demands on the famine-stricken population became inevitable, and during the closing months of the year 1939, a rather rapid deterioration in health conditions occurred. Investigations during December showed that, compared with the findings of February, the population as a whole looked more poorly fed, the minor effects of qualitative food deficiency were much more readily detectable, fully developed acute deficiency disease (scurvy) had made its appearance, and many individuals in the areas worst affected by the famine were suffering from frank starvation of varying degrees. This decline in health was much more marked among those remaining in their villages than amongst workers at relief works.

#### *Preventive and curative measures—germinated grain as a prophylactic against scurvy*

In devising means to meet the worsened health conditions it was recognized that the problem was to a large extent physiological. Other facts being constant, food requirements are proportionate to energy expended and in cold weather relatively more food is required to maintain body temperature. These fundamental principles had to be taken into consideration in the first instance. The task of workers was therefore reduced by 50 per cent from the end of January 1940, and new works were organized so that villagers did not have to walk long distances to and from their work. Weakly individuals were relieved of work altogether. In addition, the health organization, both curative and preventive, in rural areas was rearranged and expanded. The district was divided into a series of 50 health circles, each in charge of a medical officer, a circle including the villages within 5 miles of a central dispensary. Special treatment centres were established to which the acutely ill, whose condition allowed of their being moved short distances, were evacuated for care and treatment, and arrangements were

made for the regular visiting of sick in villages by the medical officers of dispensaries and treatment centres, who were required to tour regularly in their circles and make systematic search for sick people.

The most important specific preventive measures adopted to check the development of deficiency disease were the introduction of germinated grain as a prophylactic against scurvy, and of the Indian gooseberry (*amla*) for the treatment of that disease. The *amla* was advocated by Dr. W. R. Aykroyd, Nutrition Research Laboratories, Coonoor, following the work of K. V. Giri (1939) on Indian gooseberries (*Phyllanthus emblica* Linn.) as a source of vitamin C.

During the latter part of December 1939 and January 1940, specific measures were limited to the treatment of developed cases of deficiency disease. It was found that scurvy in the most acute form and advanced degree responded rapidly to treatment with *amla* juice.

It was not until the first week of February 1940 that regular issues of germinated grain to all labour on relief works were commenced. The free issue consisted of half a *chhatak* (1 ounce) of germinated wheat, millet, or gram twice a week, and in many villages the inhabitants were persuaded to prepare this prophylactic for themselves. By the middle of February more than 200,000 individuals were taking this protective food regularly.

From 27th May women and children ceased to attend relief works except once a week to receive their gratuitous relief pay, and on that occasion were given one *chhatak* of germinated grain each.

Germinated grain has much to commend it as a preventive against food deficiency conditions. Grain in some shape or form is available everywhere, and the procedure for producing germination is simple. The people are already familiar with grain in this form, as it is partaken of at certain festivals, and it does not offend religious susceptibilities. It contains vitamins A and B, and particularly C in abundance, and small quantities added to an otherwise defective diet make good what is lacking.

#### *Results of preventive measures*

The famine began in 1938 and its general effect on health may perhaps be gauged more accurately from a consideration of mortality figures than by any other means:—

Number of deaths in Hissar district			
1937	..	..	20,910
1938	..	..	28,505
1939	..	..	37,767

If mortality figures for the first six months of the years 1937 to 1940 be compared, an

approximate idea may be obtained of the results of the curative and preventive measures applied :—

	Deaths			
	1937	1938	1939	1940
January ..	1,746	2,052	3,885	2,299
February ..	1,619	1,587	3,193	1,918
March ..	1,607	1,961	3,036	2,177
April ..	1,783	2,564	3,096	2,643
May ..	2,101	4,225	4,101	3,290
June ..	2,168	3,730	4,026	2,982
TOTAL ..	11,027	16,119	21,337	15,309

That there should be a reduction, compared with the previous year, of over 6,000 in the number of deaths in the first six months of what was really the third year of continued famine is significant. Not only had the downward trend been arrested but a definite positive improvement had been effected.

A consideration of the actual number of cases of sickness admitted to hospitals, dispensaries, and treatment centres, and the number of cases attending as out-patients at dispensaries, may indicate the extent to which specific measures against deficiency disease were effective.

*Morbidity in Hissar district—December 1939 to June 1940*

	Total sick admitted to hospitals and dispensaries	Cases of scurvy admitted (new cases)	Cases of night-blindness out-patients attending (new cases)
December 1939 ..	523	67	1,412
January 1940 ..	696	80	746
February " ..	421	60	1,282
March " ..	452	9	1,167
April " ..	446	..	883
May " ..	354	..	895
June " ..	332	..	1,007

The general decline in sickness of such a severity as to warrant admission of the individual to hospital, dispensary or treatment centre is marked.

The dramatic disappearance of scurvy after the introduction of germinated grain in the first week of February is very striking. From January 1940 onwards, villages were systematically combed for cases of this disease.

A reduction in the number of cases of night-blindness attending as out-patients occurred, but the fact that so many cases were still reporting sick during the month of May and that there was an actual increase in June, indicates that germinated grain, as might be expected, was not in the same degree a preventive of this condition as of scurvy.

There were on an average 35 cases of malnutrition, other than night-blindness and scurvy, being admitted to hospitals and dispensaries every month during the first six months of 1940. A consideration of these cases, together with the persistence of night-blindness, suggests that the

almost entire absence of animal fat from diets was making itself very definitely felt. The fact that tuberculosis and other infections began to appear more frequently as causes of death during this period points in the same direction, but it cannot be definitely stated that there was an increase in these diseases owing to the fact that from January 1940 diagnoses were more accurate than they had been during the corresponding period of 1939, when the majority of sick people were not seen by a doctor and many cases of these diseases were almost certainly missed.

During the first six months of 1939, there were 481 deaths from smallpox in Hissar district. During the corresponding period of 1940, the number had fallen to 79. A total of 184,921 vaccinations were performed between November 1939 and the end of June 1940. The vaccination campaign was just as vigorously carried on during 1938-39, but the reporting of cases was very defective at that time: in 1940 the fact that villages were being regularly visited by medical officers resulted in cases coming to light immediately on their occurrence, and preventive measures could consequently be much more quickly and effectively applied.

In the spring of 1940, for the second year in succession, mass anti-cholera inoculation was carried out amongst workers: by the end of June 193,874 anti-cholera inoculations had been given. Cholera was absent from the district in 1939 and had not appeared up to the end of July 1940.

From the foregoing, I think one is justified in believing that the major epidemic and deficiency diseases were brought under control, and that the specific preventive measures introduced were not ineffective. Lesser degrees of malnutrition were, however, still prevalent at the end of June 1940, resistance to disease in general was apparently low, and health conditions extremely unstable.

Throughout 1939 the effect of the famine on the mentality of the people was very noticeable: there was an air of depression throughout the community and many seemed completely indifferent to what happened to them. The lifting of this depression was one of the most striking results of the expansion and extension of health measures.

*Famine conditions and mortality*

Innumerable statements regarding death rates in the famine areas have been published, many of them grossly exaggerated and most of them misleading. A few figures may serve to bring mortality in Hissar into proper perspective.

*Deaths in Hissar district*

Average annual number of deaths, 1934-38	Actual deaths, 1939
24,794	37,767



*Deaths in the young and old in Hissar district*

	AVERAGE NUMBER	ACTUAL NUMBER		
	1934-38	1937	1938	1939
Under 10 years	11,044	11,764	16,854	21,160
60 years and upwards.	2,372	2,779	3,973	6,836

It will be observed that the brunt of the famine fell on the young and the old. 74.1 per cent of the total deaths occurred in individuals under 10 and over 60 years of age. For every 100 males who die, 114 deaths occurred amongst females, as compared with an average of 107 during the preceding five years.

*Causes of death*

Of the 37,767 deaths, no fewer than 30,522 were registered as due simply to 'fevers'. Smallpox was given as the cause of 480 deaths, diarrhoea and dysentery of 627, enteric fever of 854, tuberculosis of 567, and pneumonia of 1,172.

Compared with the average for the years 1934-38 the number of deaths from pneumonia and other respiratory diseases was more than doubled during 1939, and dysentery accounted for nearly twice as many. As compared with the figures for 1934-38 nearly 12,000 more individuals died from 'fevers'.

Cholera and plague were absent from the district. Deaths from smallpox occurred during the early months of the year, but by the month of May the disease had been brought under control and did not appear again as a significant cause of death throughout the remainder of the year.

A contributory cause of the increased death rate was the fact that numbers of families, particularly Rajputs—both Hindu and Muslim—considered it beneath their dignity to accept Government relief which they regarded as 'charity', or to bring themselves or their women folk to associate with what they were pleased to regard as 'coolie labour' on relief works.

It is of interest to compare the 1939 mortality figures for Hissar district with those for 1900, which was a year of famine in some degree comparable in severity to that of 1930.

	Actual number of deaths	Death rate	DEATHS FROM PARTICULAR DISEASES		
			Cholera	Dysentery	'Fevers'
1900 ..	74,798	96.4	6,399	2,823	54,324
1939 ..	37,767	42.0	Nil	638	30,522

These figures may be regarded not only as evidence of the greater effectiveness of famine relief measures, but also of the greater control

over disease in general, which has been developed since the beginning of the present century.

Very few of the 37,767 individuals who died during 1939 were seen by a doctor during their final illness (there were only 201 deaths in hospitals and dispensaries), since most of them occurred in villages in which there are no doctors, and not until the end of the year were arrangements made for doctors to tour in rural areas. Careful inquiry has elicited information regarding the character of the last illness in certain areas, particularly in families in which several members died, and in which the survivors were found to be suffering from acute scurvy. The survivors were most emphatic in maintaining that their relatives who had died had the same complaints and showed the same outward signs of illness as themselves.

It is probable that many of the deaths recorded as due to 'fevers' were really caused by starvation and deficiency disease, and that many of the pneumonias and dysenteries were merely terminal illnesses in individuals primarily suffering from malnutrition.

*Morbidity*

Reliable information regarding the character of the illness from which people suffered can be obtained only from the records of hospitals and dispensaries in which diagnoses are made by qualified medical practitioners. The number treated at such institutions rose from 440,582 in 1937 to 479,182 in 1938 and 557,916 in 1939. The majority of these individuals were out-patients, only 8,328 in-patients being treated during the year 1939.

If we may regard the approximate half million of patients who attend at or are admitted to hospitals and dispensaries in a year, as a representative sample of the sick population throughout the district, then certain tentative deductions may be made regarding morbidity. Table III gives the chief causes of illness in patients of this class. The figures are from the official records of the inspector-general of civil hospitals.

The illnesses from which by far the larger proportion of patients suffered remained practically the same over the three-year period. The increase in number in the larger groups (numbering 10,000 or more) is progressive, and the rate of increase fairly uniform, the only notable exception being in the case of malaria.

In these larger groups the striking increase in diarrhoea and dysentery in 1939 is noteworthy. An interesting point is that these larger groups, which include by far the majority of sick people who sought treatment, do not include the specific food deficiency diseases, or illnesses such as tuberculosis which are known to tend to increase as a result of malnutrition. The increase in these larger groups might be regarded as indicating the occult effect of malnutrition in lowering resistance to disease in general, and to prevalent infections, such as dysentery, in particular.



TABLE III

*Chief causes of illness in patients treated at hospitals and dispensaries in Hissar district, 1937-39*

	1937	1938	1939
Eye diseases (excluding trachoma, glaucoma and cataract).	63,951	70,914	83,659
Respiratory diseases (excluding pneumonia and pulmonary tuberculosis).	25,178	32,357	41,117
Malaria .. ..	34,553	27,301	35,537
Trachoma .. ..	21,031	22,911	26,550
Diseases of the digestive system (excluding diarrhoea, dysentery and tumours).	19,398	21,136	25,996
Injuries .. ..	21,847	23,926	25,331
Diseases of teeth and gums (excluding tumours).	15,985	18,526	20,188
Diarrhoea and dysentery ..	10,268	11,936	19,907
Diseases of the intestines (excluding diarrhoea, dysentery and tumours).	13,254	15,425	19,186
Diseases of the stomach (excluding tumours).	10,491	12,322	16,309
Diseases of the nervous system.	11,048	12,963	14,358
Diseases due to deficiency or to disorders of nutrition or metabolism (excluding osteomalacia, rickets and scurvy).	568	545	9,160
Pyrexia of uncertain origin and other diseases due to infection.	2,925	3,922	5,216
Diseases of the blood and spleen.	1,692	1,588	2,117
Pneumonia .. ..	1,409	1,707	1,942
Tuberculosis of lungs .. ..	696	652	973
Tuberculosis (non-pulmonary)	762	724	912
Enteric fever .. ..	282	272	539
Rickets .. ..	160	123	208
Scurvy .. ..	52	4	116
Osteomalacia .. ..	40	77	75

When we come to consider the disease groups or individual diseases in which the numbers are relatively smaller (under 10,000) the points of interest are the increase in pyrexia of uncertain origin and other diseases due to infection, pneumonia, and diseases of the blood and spleen, and the enormous increase in 1939 in unspecified disorders of nutrition or metabolism. Compared with the latter the specific deficiency diseases are small in number.

The progressive increase in tuberculosis, both pulmonary and non-pulmonary, and the increase in enteric fever in 1939 are striking.

#### *Summary and suggestions*

Even when adequate relief in the form of relief pay is provided, the ill effects of famine are likely to be felt acutely and at an early stage, if individuals be left to themselves to procure their food from stocks available locally.

Under such conditions a progressive deterioration in health is to be expected and this may be hastened by conditions which make increased demands on energy.

Fully-developed deficiency disease such as scurvy may be a later feature of deterioration in the health of the community, but prior to its appearance death rates from other causes are likely to have increased greatly. The young and the old are likely to suffer most severely from famine, and women more than men.

The approach to famine relief work should be along physiological lines. In the past the primary and main objective has been to provide the individual with means for obtaining a certain quantity of food. This alone is likely to be to a great extent ineffective in maintaining health: arrangements should be made for the individual to procure food of the right kind; money spent will be largely wasted if a sufficiency of the protective foods—particularly fresh green vegetables and animal fat of some kind—be not made available.

Even the quantity of food required will depend on energy expenditure. An individual can get along on remarkably little if he be simply sitting about at home. His requirements are vastly increased if he has to perform manual labour all day and walk 5 to 10 miles to and from his work. The ideal would be the elimination of relief works altogether, but as this does not appear to be feasible for administrative reasons, the task prescribed should be nominal and the place of work within easy reach.

In the Punjab, the relief allowance for growing children and adolescents is a quarter and a half, respectively, of an adult allowance, yet the physiological needs of these two groups are relatively greater than those of adults, if growth and development are to be maintained at a normal rate and deficiency disease kept at bay. The same applies to child-bearing women and nursing mothers. Scales of wages and allowances should be arranged accordingly, and the allowances for a family should be calculated on the number of adult male consumption units composing the family.

In arranging for the maintenance of animals in a famine area, due regard should be paid to conserving the milk supply. Present practice in the Punjab is for the villager to retain a pair of ploughing bullocks and one milk animal, and Government supplies fodder for these. Other milk animals have to be sold or sent to a cattle concentration camp. At these camps many cows and buffaloes bear calves and become milk producing. The preservation of the existing milk supply would appear to be the only practicable method of making animal fat available to a large famine-stricken population, quite apart from its food value in other respects. It seems reasonable to suggest that the maintenance of milk animals in villages should be a first consideration in planning famine relief. The supply of fodder by Government could be made conditional on an equitable distribution of milk

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# FURTHER NOTES ON THE APPLICABILITY OF THE VITAMIN-C TEST OF URINE IN ESTIMATING HORMONAL VARIATIONS IN THE SYSTEM

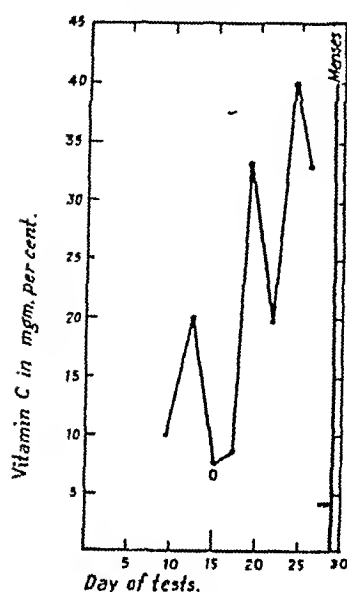
By A. P. PILLAY, O.B.E., M.B., B.S.

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In the paper (Pillay, 1940) I answered in the affirmative the question—Does the quantitative estimation of vitamin C in the urine help to decide the day of ovulation? The following additional interesting findings based on the same test have since been observed by me:—

GRAPH 1

After 300 mgm. of Redoxon for each test.



the affirmative the question—Does the quantitative estimation of vitamin C in the urine help to decide the day of ovulation? The following additional interesting findings based on the same test have since been observed by me:—

(i) During the luteal phase of the menstrual cycle, the excretion of vitamin C in the urine is higher than during the follicular phase. Graph 1 illustrates this point.

(Continued from previous page)

throughout a village community (in accordance with the needs of individual families. Even from the limited view-point of economy, in a famine area it does not seem sound practice drastically to reduce supplies of the most important of all articles of diet and one which the community is producing within itself.

The conservation of existing food supplies in the area and arrangements for individuals obtaining a sufficient quantity of food of the right kind constitute the first line of defence against the effects of famine. Even when this has been achieved, the occult influence of minor degrees of malnutrition, both qualitative and quantitative, in lowering resistance to disease, is likely to make itself felt. Every means of guarding against infections should therefore be systematically applied—general environmental sanitation including chlorination of water-supplies, specific measures directed against individual diseases (vaccination, anti-cholera and anti-typhoid inoculation) and, should circumstances require, the issue of prophylactics calculated to ward off specific food deficiency disease.

Germinated grain is an effective preventive of scurvy when given in quantities of 1 ounce (dry grain) per head twice a week.

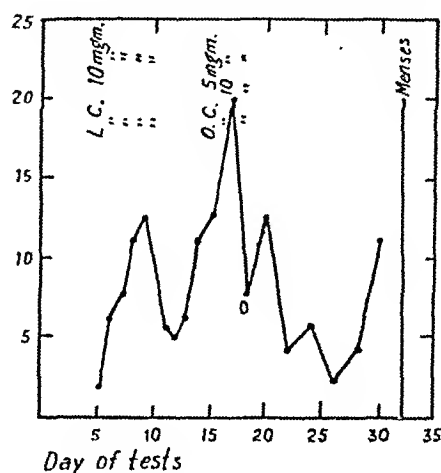
## REFERENCE

Giri, K. V. (1939). *Indian Journ. Med. Res.*, Vol. XXVII, p. 429.

(ii) There is vast difference in the amount of vitamin C excreted in the urine when progesterone and oestrin are administered, large quantities being excreted during progesterone administration and smaller quantities during oestrin administration. Graphs 2 and 3 illustrate this conclusion. Graph 2 is that of a case of severe secondary amenorrhoea and graph 3 that of a case of virilism.

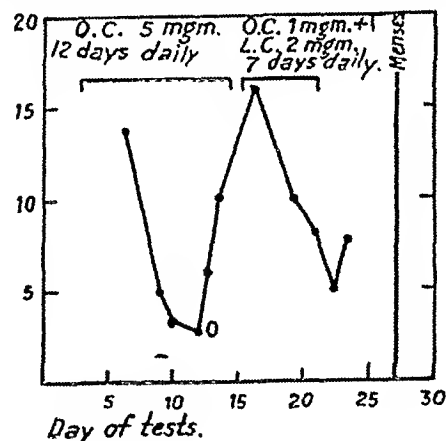
GRAPH 2

After 200 mgm. of Redoxon for each test.



GRAPH 3

After 300 mgm. of Redoxon for each test.



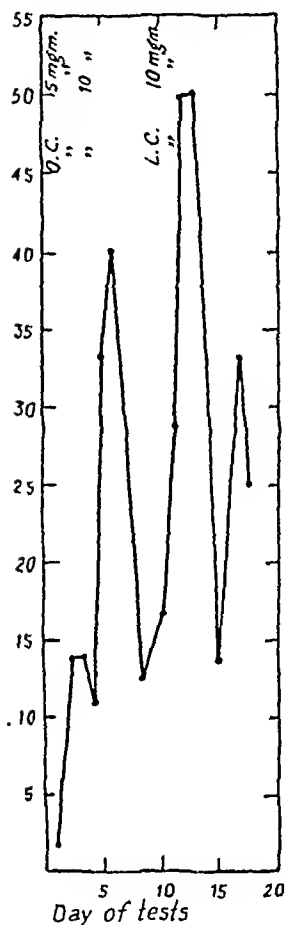
These findings make it legitimate to conclude that the estimation of vitamin C in the urine forms a method of gauging the amount of progesterone and oestrin present in the system.

At this stage of the investigation it will be rash to attempt to explain how and why this is so. The following possible explanations, among others, are offered. When progesterone is present in excess in the system, as during the luteal phase of menstruation or when it is administered, the body requires or retains only small quantities of vitamin C. When progesterone is absent or deficient, as during the follicular phase of menstruation or when oestrin is administered, the system requires or retains large quantities of vitamin C. It might also be that progesterone takes the place of vitamin C or otherwise acts as a tonic on the system and dispenses with the necessity for large quantities of

this essential vitamin. That the same variation in the excretion of vitamin C is seen in the male also during the administration of progesterone and œstrin lends colour to this (graph 4).

GRAPH 4. MALE

After 200 mgm. of Redoxon for each test.

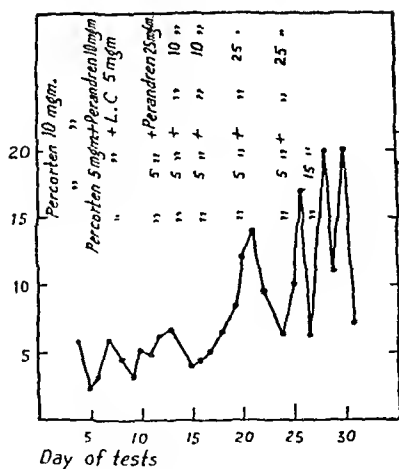


The horizontal lines in the graphs indicate the days of the menstrual cycle, unless otherwise stated. The hormones were administered in all cases by injection. O stands for ovulation, O.C. for Ovocyclin (Ciba), L.C. for Luto-cyclin (Ciba).

If progesterone acts on the system as a tonic, the interesting question arises as to whether any other hormones act likewise and have similar effects on the vitamin-C excretion. Graph 5 is that of an elderly, æsthenic male during administration of adrenal cortex hormone (Percorten, Ciba) and testicular hormone (Perandren, Ciba). The æsthenia steadily improved when the system was 'soaked' with these hormones and concurrently the vitamin-C excretion in the urine increased.

GRAPH 5. MALE

After 100 mgm. of Redoxon for each test.



What causes the decolorization of the dye solution is also difficult to dogmatize on. If it is not due to vitamin C itself, it may be that

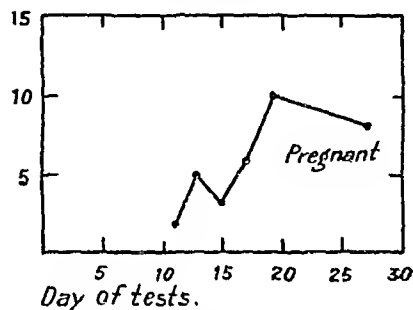
progesterone (or its excretion product, pregnandiol) decolorizes the dye solution or it liberates some other, as yet unrecognized, substance in the urine which causes the decolorization.

Whatever may be the explanation, the tests with vitamin C have many practical applications, such as estimating the deficiency of either of the ovarian hormones, their doses for therapeutic purposes, the time required to produce the maximal effect with them and so on.

(iii) According to Wilson, Randall and Osterberg (1939) large amounts of pregnandiol in the urine of a regularly menstruating woman immediately after she misses a period is indicative of pregnancy. Based on my findings, this means that the vitamin-C excretion in the urine should be consistently high in cases of early pregnancy. Estimation of vitamin-C excretion in urine is therefore a test for diagnosis of early pregnancy. Graph 6 illustrates this conclusion.

GRAPH 6

After 300 mgm. of Redoxon for each test.



There were a few atypical cases in my series, with low excretion of vitamin C during the luteal phase, but these only indicate a deficiency of progesterone in the luteal phase and not a fallacy in my conclusions. I consider the atypical cases lend support to my contention that the vitamin-C test gives the measure of the deficiency of progesterone in the system.

The results of my experiments on the practical application of the vitamin-C test in diagnosis and treatment of conditions such as amenorrhœa and sterility due to normal defects will be published in due course.

#### The vitamin-C test

The test is done as follows: The woman is given orally 300 mg. of vitamin C (Redoxon, Roche) three to six hours before the test. One tablet of dichlorophenol-indophenol (Roche) is dissolved in 50 c.cm. of water. Five c.cm. of the solution is pipetted into a beaker. Freshly voided urine is titrated quickly into this solution from a burette and the quantity required to decolorize immediately the blue of this solution gives the quantity of vitamin C present in the sample of urine. The test should be completed within two minutes after the urine is passed.

In my earlier experiments I used to give 300 mgm. of Redoxon before every test. Now I give this dose only before the first test to estimate the actual deficiency of vitamin C in the system. The dosage for the further tests is

(Continued at foot of next page)

## GASTRIC ACIDITY IN CHOLERA

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As vomiting is one of the prominent symptoms of cholera it was thought desirable to determine

*(Continued from previous page)*

decided for each case after noting the amount of initial deficiency. 150 to 200 mgm. are found to be sufficient for the follow-up tests in most cases, provided the initial vitamin-C deficiency is corrected. Unsurcharged urine is apt to give fallacious results as its vitamin content is liable to be affected by variations in diet and other factors. With urine highly surcharged with vitamin C, the daily variations of its excretion may often be so small as to be overlooked if very careful observations are not made.

In the graphs published with my first paper, the vertical lines indicated the quantity of urine in c.cm. required to decolorize 5 c.cm. of the dye solution, while in the graphs given here, the vertical lines indicate the vitamin-C content of the urine in mgm. per cent. This is arrived at by dividing 10 by the quantity in c.cm. of the urine required to decolorize 5 c.cm. of the dye solution, which is equivalent to 0.1 mgm. of l-ascorbic acid.

*Summary*

Estimation of vitamin C in the urine helps in deciding

- the day of ovulation,
- the type of the cycle, whether anovulatory, uniovulatory or multiovulatory,
- the deficiency of either of the ovarian hormones in the system,
- the dose of ovarian hormones required for therapeutic purposes,
- the time the ovarian hormones takes to produce maximal effects,
- the effects and progress of hormone therapy, and
- whether a woman who has missed a period is pregnant.

*Acknowledgment*

For this study, hormones were supplied by Messrs. Ciba Ltd., and Redoxon and the dye tablets by Messrs. Hoffmann-La-Roche Ltd. and I am grateful to their representatives in India for this help.

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whether, on recovery from the disease, there is any evidence of impairment of digestive function (as judged by a test meal). In this paper are recorded the results of the examination of 25 cholera patients.

In order to avoid variable factors of age and sex in the subsequent analysis only males between the ages of 18 and 35 years were examined. The patients were of the labouring class and those selected for examination were moderately well built and not suffering from any apparent anaemia.

The test meal examination was made on the day of discharge from the cholera ward, when patients were able to walk about and were on ordinary diet—usually 7 to 10 days after the onset of the disease. In 17 patients the diagnosis was confirmed by the isolation of *Vibrio cholerae* from the stools during the acute stage of the disease and in the remaining eight, in whom *V. cholerae* had not been isolated from the stools, agglutinins in significant titres for *V. cholerae* were demonstrated in blood taken on about the tenth day of convalescence. In all patients the attack of cholera was clinically typical but comparatively mild. There had been vomiting during the acute stage of the disease, but this had not been as copious nor as frequent as in the more severe types of the disease.

The alcohol test meal was used. After the fasting stomach contents had been withdrawn, 50 c.cm. of 7 per cent alcohol in distilled water was injected into the stomach through a Ryle's tube. About 10 c.cm. samples of gastric juice were withdrawn every fifteen minutes up to a maximum of 10 samples. The samples were examined for free hydrochloric acid and total acid by titration with decinormal caustic soda solution, using Topfer's reagent and phenolphthalein as the indicators. Further examinations, as for example for acid deficit (or the amount of acid which must be added before a test for free hydrochloric acid is obtained) in samples which had no free hydrochloric acid, and for the presence of enzymes (pepsin and rennin), were made, according to methods described by Levinson and MacFate (1937). In this paper only the free acid is considered.

The results have been classified according to the grouping adopted by Napier *et al.* (1938) and are shown below.

Hyperchlorhydria—Over 65 c.cm. of N/10 NaOH per 100 c.cm.

Normal range High—over 45 but under 66.

Average—25 to 45.

Low—under 25 but not below 10.

Hypochlorhydria—Below 10 c.cm.

Achlorhydria.

According to this grouping the results obtained in 25 cholera patients are:—

Hyperchlorhydria— None

Normal range—

High	None
Average	3 or 12 per cent
Low	8 or 32 " "

Hypochlorhydria— 5 or 20 " "

Achlorhydria— 9 or 36 " "

As judged by the residual gastric juice after the fractional test meal the stomach empties more rapidly than normal in the majority of these patients.

It was not convenient to carry out a histamine test in patients with complete absence of free hydrochloric acid after the alcohol meal. As considerable persuasion was necessary to secure patients who had recently recovered from an attack of cholera to attend at the laboratory and submit to a fractional test meal, it was thought inadvisable to risk frightening any of them by injections and/or a possible severe reaction following histamine. It is hoped, however, to examine a further series of patients and to test a certain number of cases of achlorhydria with histamine.

The results show that there is achlorhydria in 9 (36 per cent) of the 25 patients examined. If we accept the incidence of 9 per cent achlorhydria (to the alcohol meal), which is the figure arrived at by Napier *et al.* (*loc. cit.*) for their non-anæmia cases (13 cases of achlorhydria in 151 cases), then the incidence of achlorhydria in 36 per cent of cholera convalescents is a finding which is unlikely to be due to chance or error of sampling. The observed difference is 2.7 times its standard error.

The incidence of low acid secretion is extremely high. An average normal range of acid secretion was present in only 3 (12 per cent) of the patients and in the rest (88 per cent) there was low acid or no acid secretion. There was hypochlorhydria or achlorhydria in more than half the patients (56 per cent). The absence of a single case of hyperchlorhydria in the 25 patients examined is by itself of significance.

The occurrence of low acid secretion in a large proportion of cases following an attack of cholera can be explained by one or more of the following hypotheses:—

1. It is the result of an acute gastritis, which leads to the development of achlorhydria or hypochlorhydria in a large proportion of cases. Hurst (1937), writing on diarrhoea, states: 'If the diarrhoea is accompanied by vomiting a test meal should be given a month after the termination of the attack even in the absence of all symptoms, as the accompanying acute gastritis may have led to achlorhydria which is likely to give rise to chronic diarrhoea or other trouble later unless the underlying chronic gastritis is overcome'.

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## THE BACTERIOLOGY OF COLD DRINKS IN CALCUTTA

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AERATED and non-aerated refrigerated drinks were examined for the number of bacteria per cubic centimetre and for the presence of *Bacterium coli*. The samples were collected from certain shops situated in different parts of the city. The non-aerated cold drinks after being served out by the vendor were transferred to an eight-ounce sterile screw-capped bottle and brought to the laboratory for examination, which was made soon after receipt of the samples. The aerated drinks were bought in the original bottles and these were opened in the laboratory at the time of the examination. The examinations were made according to methods advocated by the Ministry of Health, 1939, and are summarized below:

(Continued from previous column)

2. It is one of the sequelæ of the state of anhydræmia which follows loss of water, acid, and neutral chlorides during the acute stage of the disease.

3. It is the result of a natural selection that has taken place in the sample of cholera convalescents. This presupposes that the disease occurred in individuals who at the time of infection with *V. cholerae* had deficient acid secretion in their stomachs and that those with high normal or hyperchlorhydria escaped infection. Whether such natural selection occurs is difficult to establish.

It is hoped to follow up some of the cases and to determine by repeated test meal examinations whether the gastric juice returns to normal, particularly in cases showing achlorhydria.

### Summary

In 25 individuals who had recovered from an attack of cholera, achlorhydria (after a standard alcohol test meal) was found in 9 or 36 per cent, hypochlorhydria in 5 or 20 per cent, low normal acid curve in 8 or 32 per cent and an average normal acid curve in 3 or 12 per cent.

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## (A) Presumptive coli test.

The sample bottles were shaken twenty-five times before removing portions for examination, which were inoculated as follows:—

Fifty c.cm. into a fermentation tube containing 50 c.cm. of double-strength MacConkey's broth (lactose bile-salt neutral-red broth).

Ten c.cm. into each of five tubes containing 10 c.cm. of double-strength MacConkey's broth.

One c.cm. into each of five tubes containing 10 c.cm. of single-strength MacConkey's broth.

The tubes were incubated for 24 hours at 37°C. and the results noted. If there was no gas formation the tubes were reincubated for another twenty-four hours. Platings were made on MacConkey's neutral-red bile-salt lactose agar from four of the tubes showing the greatest volume of gas. After incubation for twenty-four or forty-eight hours colonies suggestive of the coliform group were selected and a part of each colony transferred to peptone water, two tubes of glucose phosphate broth and citrate medium for the indole, Voges-Proskauer and methyl red, and the citrate utilization tests. The most probable number of coliform bacilli are computed according to the probability tables given in the Ministry of Health report (*v.s.*).

## (B) Total colony count.

With non-aerated drinks 1 c.cm. of a 1 in 10 and 1 c.cm. of 1 in 100 dilution (made with sterile tap water) were plated. In the case of aerated drinks 1 c.cm. of the undiluted sample and 1 c.cm. of a 1 in 10 dilution were plated. For each plate at least 12 c.cm. of nutrient agar was used and the agar after melting was maintained in the melted condition in a water-bath at 45°C. before seeding and pouring. The plates were incubated for forty-eight hours and the plates that contained between 30 and 300 colonies were counted under standard conditions. The average of the duplicate plates multiplied by the dilution factor was taken as the number of bacteria per cubic centimetre of the sample.

A total of 42 samples of cold drinks was examined, of these 22 were samples of non-aerated drinks and 20 of aerated drinks. The standard taken for comparison was that the number of bacteria per cubic centimetre should not exceed 100 and that *Bacterium coli* should be absent in 100 c.cm. or if present be not more than two coliform organisms per 100 c.cm. of the sample. This is based on the classification of non-chlorinated piped water supplies recommended by the Ministry of Health (*loc. cit.*) and reproduced below:—

	Presumptive coliform count per 100 c.cm.
Class 1. Highly satisfactory ..	less than 1
Class 2. Satisfactory ..	1-2
Class 3. Suspicious ..	3-10
Class 4. Unsatisfactory ..	greater than 10

According to the above grading not one of the 22 samples of non-aerated drinks examined would be considered satisfactory. Two samples were of class 3 and the remaining 20 samples fell in class 4. The majority of such samples gave a presumptive coliform count of 180 or over. Coliform organisms of the faecal type (*Bact. coli* type I from eight samples and type II from one sample) were isolated from 9 (41 per cent) of the 22 samples of non-aerated drinks. Members of the intermediate-aerogenes-cloacæ group were isolated from the majority of the samples with

yeasts predominating in the sweeter drinks. The colony count (plate incubated at 37°C.) was about 1,500 colonies per c.cm. in two samples and more than 3,000 colonies per c.cm. in the remaining 20 samples.

According to the results of the presumptive coli test the 20 samples of aerated drinks were of the following classes—

Class 1. Highly satisfactory ..	6 samples
Class 2. Satisfactory ..	2 "
Class 3. Suspicious ..	4 "
Class 4. Unsatisfactory ..	8 "

No faecal type of coliform organism was isolated from any of the samples. Organisms of the intermediate-aerogenes-cloacæ group were isolated from eight of the samples. The colony count was satisfactory (*i.e.*, below a 100) in eight samples, 250 in one sample, between 1,000 to 1,750 in three samples and more than 3,000 in the remaining eight samples. The latter were samples of flavoured and sweetened drinks.

The above results, although based on numbers too small to justify any definite conclusions, reveal (as judged from bacteriological standards) an unsatisfactory condition of the cold drinks, particularly the fruit juices and other non-aerated drinks, offered for sale to the public in Calcutta.

This finding is not surprising when it is realized that many of these drinks are prepared under conditions which cannot be considered as hygienically desirable. The aerated drinks are more satisfactory, and of these soda water appears to be best. It is interesting to note that similar results were obtained by Dzen and Chow (1936) in their examination of refrigerated drinks in Shanghai.

## Summary

Forty-two samples (22 non-aerated and 20 aerated) of cold drinks offered for sale in Calcutta were examined for the number of bacteria (colony count) and the presumptive coli test. Out of 22 non-aerated drinks examined not one sample conformed to the standard—all exceeded the permissible limit of bacteria and from 9 (41 per cent) of these samples faecal types of coliform organism were isolated. Of the 20 aerated drinks examined only eight conformed to the standard. Faecal types of coliform organism were not isolated from any of these samples.

These results, though based on a small number of samples, suggest the need for further work, the establishment of standards suitable for local conditions and the supervision and control of the manufacture of such drinks.

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# ASCORBIC ACID IN THE URINE AND ITS RELATION TO INDIAN DIETARY

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The quantitative determination of ascorbic acid is based upon the active reducing properties of the substance. The urine was titrated with the dye dichlorophenol-indophenol, each molecule of ascorbic acid reducing one molecule of the dye to its colourless leuco-base, itself being oxidized to dihydro-ascorbic acid. The method is not very accurate as there are other substances which reduce the dye, but the determination of the state of tissue saturation with respect to vitamin C is made possible by this chemical method.

The urine of 223 persons was examined. The subjects were chosen from various classes so as to give a correct idea of the nutritional condition of the people. These people were under usual dietary conditions prevalent in the district. The excretion of vitamin C in the urine of individuals on different articles of food is shown below :—

*Group 11.*—Candidates selected for a teachers' training class, well built, having good physique, doing mental work, residents of the villages of the district.

*Groups 12 and 13.*—Students of rural middle school, ages 8 to 16 years, residents of villages.

*Group 14.*—Old persons, ages 55 to 65 years. All had cataract; in a poor state of nutrition.

*Group 15.*—Residents of city. Middle class, ages 25 to 35 years. Employed in Government offices.

*Group 16.*—Students of well-to-do families. Ages 12 to 16.

*Group 17.*—A retired government gazetted officer about 62 years old.

*Discussion.*—The water-soluble vitamin C is present in urine in proportions depending on the diet and nutritional condition of the individual. The vitamin deficiency may appear either through failure of the individual to include in his diet an adequate amount of various essential foods rich in these substances or through failure properly to utilize the vitamins in diet, because of disturbances of digestion and absorption. It was observed that when the diet consisted only of rice and arhar dāl (*Cajanus indicus*) there

TABLE

Serial number	Number of persons whose urine was examined	Average weight in pounds	Diet consumed before the collection of urine	Average mg. ascorbic acid per 100 c.cm. of urine	Average daily excretion of ascorbic acid in mg.	REMARKS
1	19	119.6		1.50	15.0	The excretion was subnormal. Persons were recently drawn from villages where the diet was very poor in vitamin contents, that is, their tissues were unsaturated, and so no increase in ascorbic-acid excretion was caused.
2	15	121.6	Wheat, brinjal, potato	0.81	8.1	
3	15	116.0	Potato, gram dāl, wheat	0.61	6.1	
4	15	119.3	Wheat atta, arhar dāl (red gram), brinjal.	1.17	11.6	
5	14	112.9	Wheat, gram kulfa	1.21	12.2	increase in ascorbic-acid excretion was caused.
6	15	113.2	Rice, arhar dāl	0.68	5.9	
7	18	114.4	Arhar dāl, brinjal, wheat	1.50	14.5	
8	18	121.7	Wheat, cabbage	1.50	18.0	
9	18	..	Milk, fruits in addition to the diet of meat.	1.50	15.1	Students of urban area.
10	18	..	Wheat atta, a few had milk, dāl.	0.91	10.6	Students of middle school.
11	17	108.5	Wheat, dahi, kharbooja (melon).	3.20	31.5	Candidates for normal and training schools.
12	9	..	Wheat, dāl, curd, chana	1.91	19.1	Students of rural schools.
13	15	..	Arvi (colocasia) ghee	0.24	2.5	Old "persons" having "cataract. Well-to-do persons. Students.
14	10	..	Wheat, dāl and no vegetable	0.63	6.3	
15	4	..	Wheat, spinach, dāl	3.50	35.0	
16	2	..	Fruits	1.54	15.0	
17	1	..	Fruits with Indian daily diet	0.90	..	Low ascorbic acid. The subject was 62 years old.

*Note.*—Groups 1 to 8 were of ages ranging between 25 and 45 years. They were agriculturists of average physique and were maintained on the following diet during the period of observation—

Wheat atta—5 chatak, vegetables—2 chatak, and fat—half a tola per meal.

*Groups 7 and 8.*—Students of a Muslim high school, non-vegetarian, between 7 to 18 years of age, doing mental work.

was an excretion of ascorbic acid much below the normal (less than 15 mg. per day) (group 6). When the vegetable, brinjal, was added the excretion approached the normal (group 4). The consumption of this diet by those persons whose diet was deficient in vitamin-C content previously did not cause an increase in the excretion of ascorbic acid, showing thereby that their tissues were not saturated with vitamin C; that is, the vitamin was stored in the tissues of

such individuals (group 2). It was also observed that excretion of ascorbic acid varied in different age groups on the same diet; that is, with the increase in age there is also decrease of vitamin-C excretion (group 8 as compared with group 12). This is due to the fact that the absorption is not so efficient as in the case of young persons.

When cabbage was added to the diet urinary excretion of vitamin C rose very high (group 8). It was on an average 1.8 per cent, or roughly 18 mg. per day. Potato was found to be a good source of vitamin C in Indian dietary.

Students who were put on meat diet with no vegetable showed the output below the standard of 15 mg. per day (group 9), whereas when milk was added to the diet the excretion came up to the normal.

The age of this group was from 7 to 18 years.

In another rural school, the diet of students consisted of wheat atta, dāl (*Phaseolus mungo*), curd, gram, and arbi (colocasia). The excretion was normal (group 12). The intestines of these young persons could absorb the vitamin C of the food to the full extent, though their food was not a good source of vitamin C.

The addition of dahi (curd) to the diet helps in the absorption of ascorbic acid from the food and it is itself a good source of the vitamin. In this group (11) the average excretion was 31 mg. per day. The eating of melon also resulted in great output of ascorbic acid in the urine.

Old persons, that is, between 50 and 65 years, when put on diet containing a good quantity of vitamin C excreted ascorbic acid much below the normal (group 17).

The consumption of spinach (palak) cooked in the Indian way increased the vitamin-C content of the urine to a marked extent. The average excretion was 3.5 per cent; that is, about 35 mg. per day (group 15).

People excreting less than 1 mg. in 100 c.cm. of urine showed definite signs of vitamin-C sub-nutrition; sallow, muddy complexion, loss of energy, gingivitis, unhealthy teeth, dullness of eyes and dull, tired expression (groups 2 and 3). The tonicities of muscles was less than that of a healthy man. They were apathetic and took no interest in life. The heart sounds were feeble.

All cataract cases showed very low excretion of vitamin C in their urine. It indicates that with the diminution of metabolism on account of deficiency of vitamin C in diet, the lens is affected. The consumption of vitamin C will keep the lens in a healthy condition. The ageing processes were quick in individuals showing less excretion, that is, they looked older than their years (group 14). From the analysis of their dietary it was found that their food consisted of diet poor in vitamin C.

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## SULPHATHIAZOL IN EXPERIMENTAL STREPTOCOCCAL AND PNEUMOCOCCAL INFECTIONS

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THE present paper deals with the therapeutic action of sulphathiazol, a compound synthesized by one of the writers (Ganapathi, 1940; Ganapathi and Nandi, 1940), in experimental streptococcal and pneumococcal infections in mice.

### Methods of testing

The strains employed in the tests reported here were a pneumococcus type I strain and

(Continued from previous column)

### Conclusions

1. The vegetables of ordinary Indian diet contain sufficient vitamin C, provided they are regularly taken. Even cooked leafy vegetables produce good results. The addition of dried mango pulp in the process of cooking prevents the destruction of vitamin C of vegetables.

2. The Indian method of cooking does not destroy the vitamin-C content of the food, as is commonly supposed.

3. With the diminution of the absorbing capacity of the intestinal tract, the daily output of vitamin C in urine is very much diminished in spite of the high content of vitamin C in food.

4. There is sub-optimal intake of vitamin C in villagers as compared to the city dwellers, so special attention should be given to vitamin-C values in the daily choice and use of food in villages. This can be obtained if plenty of amaranth (chaulai), cabbage, coriander in the form of chutni, be taken daily. There are other cheap articles of food obtainable in villages, such as leafy vegetables, etc.

*Note.*—During the course of the above experiment it was found that daily output of urine in 24 hours was 800 to 900 c.cm. and the results are based on these findings.

[Ascorbic acid passed in the urine becomes oxidized in course of time. The rate of oxidation is increased by bacterial infection and by warmth. This test for ascorbic acid was devised and has been mainly used in temperate countries. In warm countries the rate of oxidation is markedly increased for two reasons, on account of the warmth itself and because warmth encourages bacterial growth in the urine.

In order to decrease this error the test must be done immediately the urine is passed, or a preservative must be used and the urine kept in a cool place.

If this is not done the results obtained will be very irregular and of little value (*vide Annual Reports of the Calcutta School of Tropical Medicine*, 1938, p. 96 and 1939, p. 108). These limitations often present an insuperable difficulty in practice.

In this paper no mention is made of the procedure adopted to prevent oxidation of the ascorbic acid in the urine.—*Error, I. M. G.]*

drug under test was made into an emulsion with gum acacia such that 0.5 c.cm. of the emulsion contained the required dose. This quantity of the emulsion was introduced into the stomach of the mouse by means of a pipette. The mice were observed for a period of 10 days in streptococcal infection and 15 days in pneumococcal infection, and the average survival time was calculated according to Whitby (1937). For comparison, tests were also put up with sulphapyridine in the case of pneumococcal infection and sulphanilamide and sulphapyridine in the case of streptococcal infection.

The following tables summarize the results of some typical experiments :—

*The therapeutic effect of sulphanilamide, sulphapyridine and sulphathiazol in experimental hamolytic streptococcal infection in mice. The drugs were administered in 10 mg. doses soon after infection and repeated 6, 24, 48 and 72 hours later*

[illegible]

*The therapeutic effect of sulphapyridine and sulphathiazol in different dosage in experimental pneumococcal (type I) infection in mice*

[illegible]

TABLE III

The therapeutic effect of sulphathiazol in experimental pneumococcal (type I) infection when administered in single and divided doses

Dosage of sulphathiazol	Number of mice out of groups of 10 dying on each day after infection											Survivals	Average survival time (days) (max. 10)
	1	2	3	4	5	6	7	8	9	10	11-15		
45 mg. once daily for 6 days.	0	0	0	0	1	0	1	2	0	1	0	5	8.3
22.5 mg. twice daily at 12 hourly intervals for 6 days.	0	0	0	0	0	0	0	0	0	0	0	10	10.0
15 mg. three times a day at 8 hourly intervals for 6 days.	0	0	0	0	0	0	0	0	1	1	0	8	9.7
Not treated (controls)	6	2	2	..	..	..	..	..	..	..	..	0	0.6

Discussion

In hæmolytic streptococcal infection sulphathiazol gives distinctly better\* results than either sulphanilamide or sulphapyridine (table I). In pneumococcal infection sulphathiazol is at least as good as sulphapyridine when administered in large doses (table II), but the results with sulphathiazol are distinctly poor when a smaller dosage is employed, due to the fact that this drug is excreted much more rapidly than sulphapyridine.

This agrees well with the findings of McKee *et al.* (1939) who have reported that sulphathiazol† when administered in 1 per cent concentration in food is as good as sulphapyridine while in 0.5 per cent concentrations it is slightly inferior. This is easily understood when we compare the blood concentrations of the drugs following their ingestion. It has been reported by van Dyke *et al.* (1939) that after a single dose of 0.5 g. per kg. in mice the maximum blood concentrations in the case of sulphapyridine and sulphathiazol are 21 mg. and 12 mg. per cent respectively, whereas with 1.0 g. per kg. doses the concentrations are 24 mg. and 26 mg. per cent respectively. So it is to be expected that with less intensive treatment sulphathiazol should be inferior to sulphapyridine, as was found by Cooper *et al.* (1939).

The drug is much more effective when given in two or three divided doses per day than when the same amount is given as a single dose (table III).

Summary

1. The therapeutic value of sulphathiazol in experimental hæmolytic streptococcal and

\* Statistical criticism of the results reported in this table does not confirm the statement that sulphathiazol is better than sulphanilamide. To establish their claims, which may be correct, though they are not supported by other workers (*see* p. 686), the writers would have to use a much larger number of mice.  
† The compound referred to by these American writers is sulfathiazole, or 2 *p*-amino-benzene sulfonamide thiazole, prepared by Fosbinder and Walter (*J. Amer. Chem. Soc.*, 1939, 61, 2032). The compound which was prepared by one of the present writers and called sulphathiazol is presumably the same compound.

pneumococcal (type I) infection of mice has been appraised.  
2. Experimental evidence presented shows that this drug is distinctly superior to sulphanilamide and sulphapyridine in streptococcal infection and is as good as sulphapyridine in pneumococcal infection.

Acknowledgment

We are indebted to Lieut.-Colonel S. S. Sokhey, I.M.S., Director, Haffkine Institute, for his kind advice throughout the course of this work.

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LECITHINOPHILE EOSINOPHILIA AND ERROR IT MAY CAUSE IN CASES OF TUBERCULOSIS AND ASTHMA\*

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THE intention is to draw attention to some cases of eosinophilia whose blood gives a positive or doubtful Wassermann reaction though they are not suffering from syphilis. The latter fact is established by following them up without giving treatment for syphilis. When the eosinophilia decreases or disappears the Wassermann reaction also becomes negative.

\* This paper was selected for the special tuberculosis number of this journal, issued last month, but was held over on account of lack of space.

It is proposed to designate the condition 'lecithinophile eosinophilia' in view of the affinity of the blood serum for the lecithin in the Wassermann antigen, in the reaction of complement fixation. The writer (Greval, Chandra and Das, 1940) has suggested for several reasons that the Wassermann reaction should be re-named lecithin-complement-fixation (LCF). One of the reasons is that it is looked upon, more or less, as diagnostic of syphilis and such is definitely not the case in the tropics. The condition under description is another reason.

'A wise precaution is to examine the sputum for tubercle bacilli in all cases of asthma' (Young and Beaumont, 1937). Some cases suspected or proved to be cases of pulmonary tuberculosis may be cases of lecithinophile eosinophilia also. The question then arises whether they are suffering from syphilis in addition. The writer has experience of such cases.

A toxic form of asthma is known which 'clears up when a positive Wassermann becomes negative or when diabetics become sugar free' (Rackemann, 1933): or does the positive Wassermann reaction become negative when asthma clears up?

The following illustrative cases are taken from a previous publication (Greval, Sen Gupta and Das, 1938):—

*Case 1.*—Eosinophilia associated with a positive Wassermann reaction (WR).

S., a Hindu female, aged 13 years, was admitted for low fever and cough and enlarged tonsils. She had 80 per cent eosinophils and the WR was positive. No other abnormality was detected. When her tonsils were removed the patient became afebrile. She was then given a course of arsenic injections. After six injections her WR was negative. Her total eosinophil count had also decreased to 12 per cent.

In this case, unfortunately, arsenic was given. With the quantity given, however, so rapid a change in the Wassermann reaction could hardly be effected in a case of syphilis.

*Case 2.*—Asthma associated with a positive Wassermann reaction.

C. S. W., an Anglo-Indian male, aged 29 years, was admitted for asthma—duration 12 years. Usual signs of asthma present. Examination of blood showed an eosinophilia of 45 per cent. His WR was positive. History and signs of syphilis were absent. Injections of peptone were given for asthma after the acute phase had subsided. There were no further attacks in hospital. The WR repeated was found to be doubtful. Eosinophils were now only 5 per cent. Before discharge the reaction was completely negative.

In this case no arsenic was given at all.

These cases were observed in the Carmichael Hospital for Tropical Diseases, Calcutta.

The Wassermann reaction was done in accordance with the technique of method no. 4 of the Medical Research Committee (British, now Council, 1918).

All cases of eosinophilia are not lecithinophile, nor is lecithinophile eosinophilia confined to pulmonary cases, although found in them often. Further, many cases of the condition give a

(Continued at foot of next column)

## A CHEAP FLUSH-OUT LATRINE

By T. R. RANGASWAMI, M.B., B.S., B.S.C.

CAPTAIN, A.I.R.O.

In a previous article (Rangaswami, 1940) the advantages of bore-hole latrines in villages were discussed. Although these are undoubtedly the best type of latrine for villages on account of their small cost permitting of them being made available for each household separately, they are not capable of universal application as they cannot be bored in unsuitable soils such as 'black cotton' soil, rocky ground, or very sandy ground in which they will cave in.

The writer has accordingly devised a cheap flush-out latrine the cost of which though much higher than that of a bore hole is not prohibitive if a larger number of people share in its use. It is capable of adoption in rural areas and bungalow types of houses. It has *pucca* walls, glazed earthenware closet and disposal chambers. This type of latrine is very much better than the bore-hole type.

When sub-soil water comes within a few feet of ground level there is the possibility of flies, mosquitoes and other insects breeding in an open bore-hole latrine. By this 'water-sealed' type of latrine, these dangers can be completely eliminated. Further, it has a much better appearance, and splashing of water on the users is avoided. The cost per seat is Rs. 122-8 and, assuming six individuals in a house, cost per individual is Rs. 20-7.

The nitrogen conserved will yield a return of 14 per cent on money spent which is no small

(Continued from previous column)

doubtful ( $\pm$ ) reaction which may be read as positive (+) at times.

This short communication, detached from the general subject of complement fixation in syphilis, is made with a view to emphasizing the existence of this important condition which is likely to add wrongly the diagnosis of syphilis to the diagnosis of tuberculosis or asthma.

### Summary

Some cases of eosinophilia give a false positive Wassermann reaction. When suspected or proved to be suffering from pulmonary tuberculosis they are wrongly suspected to be suffering from syphilis also. It is proposed to call them cases of lecithinophile eosinophilia.

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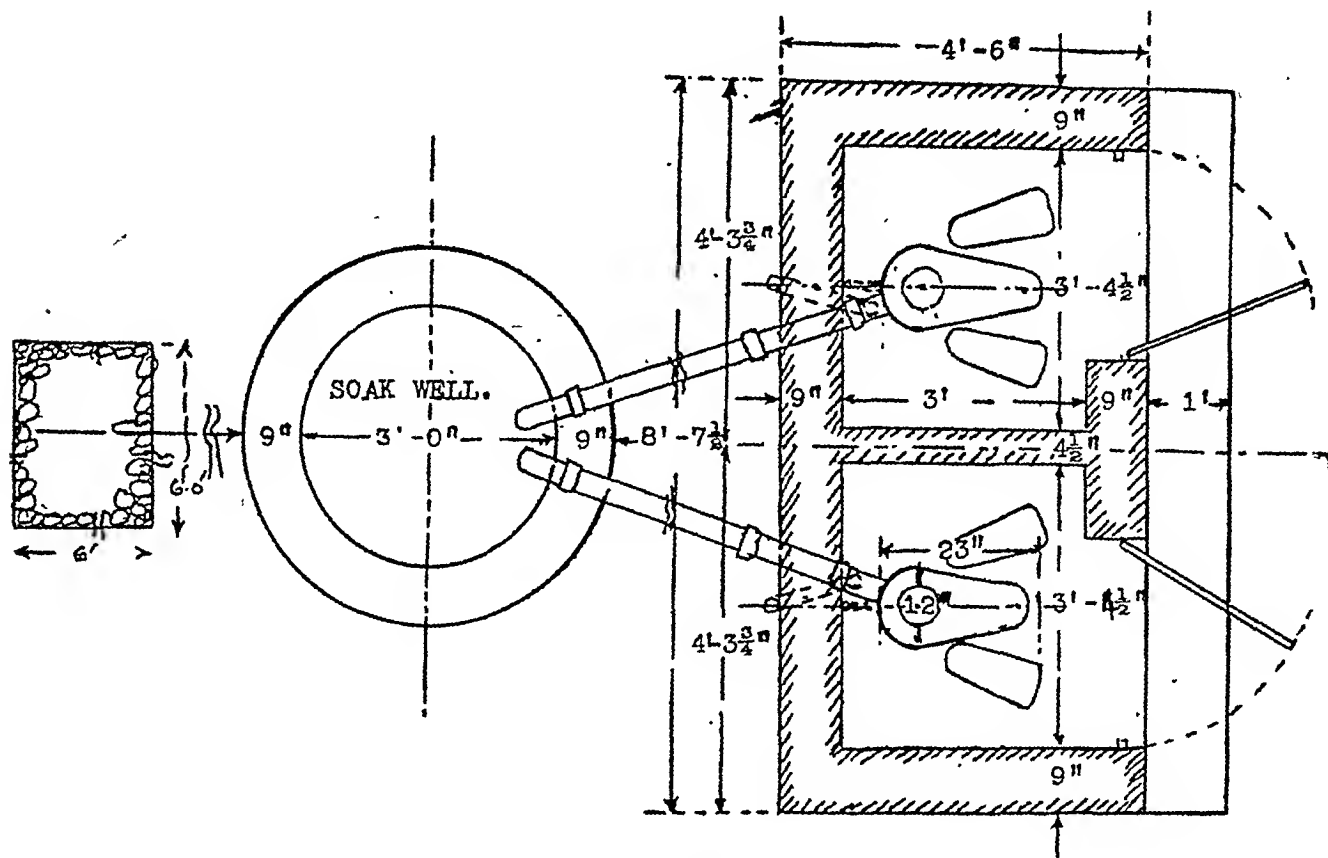
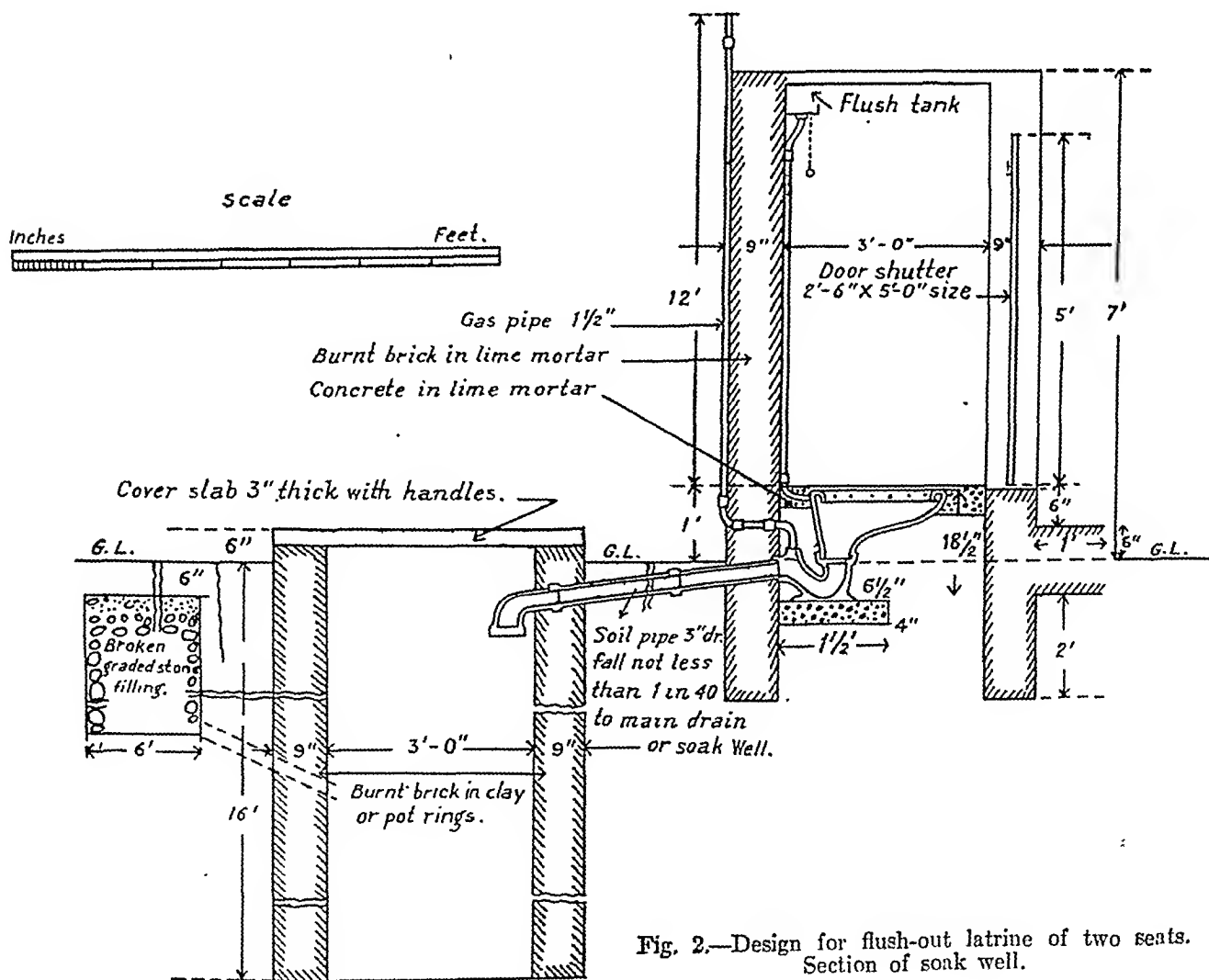


Fig. 1.—Plan.

Fig. 2.—Design for flush-out latrine of two seats.  
Section of soak well.



# A NOTE ON WELLS AS DAY-TIME RESTING-PLACES OF *ANOPHELES TESSELLATUS*

By T. RAMACHANDRA RAO  
and

PAUL F. RUSSELL

*Anopheles tessellatus* is uncommon in Tanjore District, Madras Presidency, where we have been making malaria studies (Russell, Menon and Rao, 1938; Russell and Rao, 1940). In Pattukkottai Taluk for the period of three years from March 1937 to February 1940, we found only 158 adults of that species among over 290,000 adult anophelines collected in the course of visits to dwellings of all types. In Tanjore Delta, during twelve months commencing March 1938, we collected only 17 among nearly 10,000 adults of all species taken in dwellings. It is therefore of interest to note the discovery, in December 1939, of the remarkable habit of

(Continued from page 677)

advantage, especially as the latrine problem is completely solved. Aesthetically it is distinctly preferable.

The seat is capable of easily dealing with the nightsoil and waste water from 20 people. Then the cost per seat will only be Rs. 6-2 per individual which is cheaper than a bore-hole latrine, which has been shown to cost Rs. 6-4 per individual; both estimates provide for decent permanent structures.

Thus it is cheaper than a bore-hole latrine when used for schools, colleges, factories and such other institutions, where it is sufficient to provide seats at the rate of 1 seat per 20 persons.

In his own bungalow the writer had a single-seat flush-out latrine on the lines described above with a disposal chamber only 6 feet deep and 2½ feet diameter, and this gave him entire satisfaction for about two years. Almost every month the disposal chamber was observed by opening the man-hole cover. As the writer left the station on transfer personal observations later could not be recorded. The rate of absorption was such that there was no possibility of the disposal chamber getting full. Even during a severe rain, when the compound was full of water for two days and when only the seat and step alone were above water, this worked satisfactorily.

The writer recommends a water-sealed, flush-out type of latrine, where water is readily available. In places with deficient water-supply the dry type of slab can be used and the closet-pan flooded with two or three gallons of water from a bucket, after use.

In the drawings the closet pan shown is Twyford's best English-made, Indian pattern, 23 inches in size.

Plastering is done with cement mortar.

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adults of this species of resting during day-time hours in open wells. In 25 wells which we searched and in which we found anophelines resting, we found *A. tessellatus* in 17, and were



Fig. 1.—Type of well where *A. tessellatus* was found. Exterior view.

able to collect 61 adults of this species (males 25 and females 36) out of a total of 94 adults of all anopheline species found. On one morning (13th December, 1939), 25 *tessellatus* adults were found in four wells, with only 2 adults of other species.

It should be noted that at the time the predominating species of anophelines, as judged from larva and adult collections, were *A. culicifacies*, *subpictus*, and *hyrcanus* var. *nigerrimus*, and none of these species was caught regularly in wells. If the resting of *tessellatus* in wells had been due merely to chance, *culicifacies*,



Fig. 2.—Collecting *A. tessellatus* adults in crevice in concrete-lined well. (Same well shown in fig. 1.)

*subpictus* or *hyrcanus* adults should have been found in far greater abundance than *tessellatus*. The ratio of *tessellatus* adults to the other species in wells was 2 to 1, while in collections in dwellings the ratio was 1 to 1,110.

It must also be mentioned that repeated searches of some of the wells, where *tessellatus* adults were found, failed to reveal larvæ of that species. The only larvæ regularly found in such wells were *varuna* and *culicifacies*. (Numerous culicine adults, sometimes more than

a hundred, have been found in these wells.) In over a thousand larva collections in wells in these areas, not one *A. tessellatus* was found.



Fig. 3.—Collecting *A. tessellatus* adults in crevices of brick-lined well.

This seems to indicate that the presence of the adults in wells was due to a day-time resting-place in preference.

The *tessellatus* wells were of ordinary types, having diameters of 3 to 5 feet, lined and unlined, sometimes shaded by parapet walls. In some wells where *tessellatus* was caught, there was no visible dampness at the place where they were found resting. Often they were caught in crevices in the sides, but, quite as often, on smooth vertical sides (see figures). Water levels were usually within 4 or 5 feet of the ground and there was always abundant light.

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*Footnote.*—These observations were made during routine studies of Malaria Investigations, a project under the auspices and support of the International Health Division of the Rockefeller Foundation co-operating with the Health Department of the Madras Presidency and the Pasteur Institute of Southern India in Coonoor, Nilgiris.

## A Mirror of Hospital Practice

### A UNI-OVULAR TWIN PREGNANCY WITH SPONTANEOUS DELIVERY OF A DOUBLE MONSTER

By A. V. RAMA RAO, L.M.P. (Madras)  
Assistant Medical Officer, Singareni Collieries  
Company, Ltd.

A PATIENT aged 26 years, 3rd para, was admitted to the Singareni Collieries Company Ltd. Main Hospital at Singareni on the morning of 5th June, 1940, with the history of being 8 months' pregnant. She had been in labour at her home for about six hours and the membranes had ruptured about three hours previously.



Fig. 1.

*On admission.*—The breech and two apparently normal lower limbs had delivered themselves; a few minutes later the rest of the foetus (still-born) was delivered spontaneously. It was then seen that in addition to the two normal lower limbs, there was a third lower limb projecting from the sacro-coccygeal junction with two big toes opposing each other—an indication of a fusion, which would otherwise have resulted in two lower limbs.

There were two heads normal in appearance imposed on a single trunk with normal upper limbs. In addition, there was a third upper limb springing from the back of the trunk between the two heads. This third upper limb had two hands attached in the normal position of the hand and opposed to each other. The gums of both mouths presented the appearance of having complete sets of upper and lower dentures, which had a cartilaginous feel. There were also two rudimentary male genitalia one below the other. There was only one placenta and one umbilical cord. The patient made an uneventful recovery. The photographs show anterior and posterior views of the foetus.



Fig. 2.

A skiagram was taken which showed clearly that there were two spinal columns and two sets of ribs and that the two normal-appearing arms had their origins from two separate shoulder girdles, the common arm having, apparently, no bony shoulder girdle.

I am indebted to Dr. P. M. Little, Chief Medical Officer to the Singareni Collieries Company Ltd., for permission to record this case.

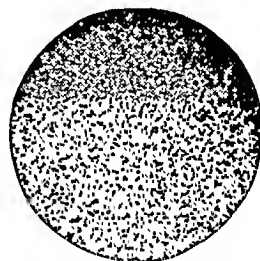


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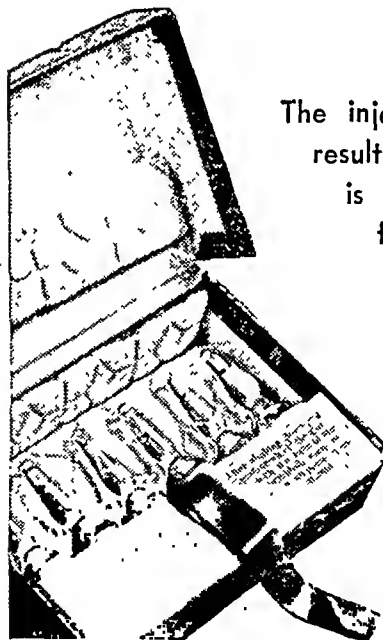
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B O M B A Y

# Indian Medical Gazette

NOVEMBER

## THE TREATMENT OF INFECTED WOUNDS

Up to the present in India we have been saved from the horrors of war, but it is by no means certain that we shall continue to enjoy this immunity; further, war is not the only source of infected wounds and with the ever-increasing mechanization and industrialization of the country the profession will be called upon more and more frequently to treat lacerated and infected wounds. Little good ever comes out of war, but on the credit side must be placed the intensive experience of the surgeon in the treatment of the infected wound. Great steps were made in the last war, the advances were consolidated during the years of peace, and further advances were made in the Spanish war, so that the prospects of the wounded soldier or civilian are considerably better in 1940 than they were in 1914.

We need not trace the progress of treatment of wounds from the time of primitive man, who probably licked his wounds like the dog does to-day, to the days of strong tissue-destroying antiseptics, if progress it may be considered, nor recount the various stages through which surgical practice passed during the last war, in which B. I. P. P. and other devices waxed and waned, but, to summarize the position at the end of the war, there were three main lines of practice, the Carrel-Dakin method of intermittent irrigation with hypochlorite or other bland antiseptic solutions, the application after free drainage of hypertonic sodium chloride or magnesium sulphate solution, paste, or even powder to ensure an active lymph flow, and, thirdly, again after free drainage, the method of immobilization, the application of abundant absorbent dressings, and non-interference for a long period. None of these three methods has yet been abandoned; in fact, the two latter methods, and particularly the last-named, have been developed considerably.

It is a matter for cynical observation that the commonest and most deadly of the bacterial flora of an established wound, the streptococcus, is introduced seldom at the time the wound is received but during the time it is being treated, and that the commonest source of infection is the nasopharynx of the patient himself or of his friends, the dressers, nurses, or doctors, for investigations have shown that the percentage of wounds infected with streptococci rises from 12 per cent to 20 per cent to 90 per cent as the wounded man passes from casualty clearing station through the base hospitals. A recent

development has, however, provided us with a means of dealing very successfully with this man-made complication and the chemo-therapeutic advances that were initiated with the introduction of sulphanilamide undoubtedly constitute the most important advance of the inter-war period in the treatment of infected wounds.

The two points about the usual war wound are that it is a lacerated wound in which considerable damage has been done to the tissues, so that they are in a very suitable condition to receive infection, and secondly that infection is abundantly provided by the clothes, soil, and other debris that were introduced at the time the wound occurred. Fortunately, there is a lag period of 4 to 12 hours from the time that the infecting organisms are introduced into the wound to the point at which they are able to establish themselves in the tissues. If therefore during this lag period we can contrive to remove all foreign and autogenous debris and infecting organisms, whilst at the same time avoiding introducing others, and approximate the cleaned edges of the wound, it will heal by first intention. 'All' is a big word and is an ideal that it is not actually necessary to achieve, for the healthy tissues of the body are capable of dealing with a considerable number of organisms, and therefore their destruction should never be pressed (*e.g.*, by the use of strong antiseptics) to the detriment of the healthy tissues; on the other hand, it is important that all foreign matter should be removed and damaged tissues cut away. The general rule is to consider that if *débridement*, as removal of the debris and cleaning up the wound is called, can be carried out within 6 hours there is a good chance that the wound will heal by first intention, that if this can be done from 6 to within 12 hours it is worth attempting to achieve primary healing, though the patient should be watched very carefully, and that if 12 hours have elapsed there is little chance that the wound will heal by first intention whatever is done and that the more extensive the *épluchage* (paring of the edges of the wound) the more harm is likely to be done in removing the tissue defences and spreading the infection.

If this early surgical treatment of the wound can be contrived the subsequent treatment of the patient consists in applying abundant antiseptic and absorbent dressings and resting the limb or part. How this can best be done, by a plaster-of-paris case, wire splints, or other means of immobilization, circumstances and to some extent the prejudice of the surgeon will dictate. Subsequently, the patient rather than the wound should be watched, and any signs, such as a high temperature, an increasing pulse rate, a general toxic appearance, or swelling and œdema of the limb beyond the wound, are indications for removal of the dressings and opening and draining the wound without further delay.

After the 12-hour safe period has passed the wound is accepted as probably an infected one and is freely opened and drained. The *débridement* in this case is conservative and only foreign matter, and obviously devitalized tissue, blood clot, etc., are removed; this is done by means of a swab with the occasional aid of a pair of scissors; the knife plays a very minor part and any cutting into healthy tissues, where a defense barrier is already established, is carefully avoided. The method of draining is again open to the choice of the surgeon but vaseline gauze, though it lacks certain very temporary advantages possessed by plain dry, antiseptic-impregnated, and salt-impregnated gauze, has other enduring qualities, namely, that it keeps the track open, does not get entangled in granulations, and is slowly extruded as the wound heals, which endear it to the surgeon. When free drainage has been ensured the wound is covered with a thick layer of absorbent dressings and the part immobilized.

It is in the subsequent treatment of the wound that there has been a change of ideas since the last war; the French practice of using plaster-of-paris has been developed considerably, first in the Winnett-Orr method of treatment of osteomyelitis and later its manifest advantages were demonstrated in the Spanish war. The general tendency now is wherever possible to encase the limb in plaster-of-paris and, ignoring the very unpleasant smell that arises as the discharges soak through the dressings into the plaster case, leave it for a week or more without further interference. The plaster may not be necessary where the patient has not to be moved, and in certain cases other means of immobilization, e.g., a Thomas' splint, may be necessary; whatever the method of immobilization the practice of non-interference is rigidly maintained. One other point is worth mentioning; whenever possible, the limb is elevated to obviate, or reduce, œdema and ensure a good blood supply.

The next important modification of procedure, and one whose potentialities have not yet been fully explored, has been provided by the intro-

duction of the sulphanilamide group of drugs. The systematic administration of sulphanilamide to all the wounded may not yet be the accepted procedure, but it has more advocates than opponents. The dose given is 1.5 grammes, *statim*, in 1 per cent citric acid to ensure rapid absorption, followed by 0.5 gramme two hours later, 0.5 gramme four-hourly for the next 24 hours and then 1 gramme eight-hourly to the end of the fourth day.

In a case where *débridement* is undertaken at an early stage, an alternative and possibly preferable measure is to powder the wound freely with sulphanilamide, introducing anything up to 15 grammes of the drug, for, not only has the drug a direct action on the organisms infecting the wound, with which it comes in contact, but the absorption of this amount of the drug into the general circulation makes the oral administration for the next 48 hours superfluous.

In a case of established infection in which prophylactic sulphanilamide has not been given a dose of 1 gramme hourly in citric acid solution for three doses followed by the usual therapeutic dosage by mouth will be far more effective than local application, for the drug might not be absorbed in the presence of much purulent discharge. The action of sulphapyridine on organisms other than streptococci, including the organisms of gas gangrene, is greater than that of sulphanilamide but the danger of the complication of vomiting after the former drug adjusts the balance in favour of the latter for routine use.

Recent experience with the wounded evacuated from France appears to have justified amply the prophylactic use of sulphanilamide, as wounded men who had received no surgical treatment arrived in England in far better condition than did men in 1918, and in the trying circumstances of the evacuation from Dunkirk the advantages of plaster-of-paris over other means of immobilization were well demonstrated.

(An important series of articles on this subject appeared in *The Lancet* from 30th March to 1st June this year.)

## Medical News

### TUBERCULOSIS ASSOCIATION OF INDIA. (TUBERCULOSIS NEWS)

#### TRAINING COURSES

THE Tuberculosis Association of India, with the co-operation of the Bombay Province Anti-Tuberculosis Association, will organize a medical postgraduate course for training in tuberculosis in Panchgani and Wanlesswadi, from the 13th January to 1st February, 1941, both dates inclusive. During the first two weeks lectures and practical demonstrations will be held in Bombay at the Seth G. S. and Grant Medical Colleges and other institutions and during the third week at the Tuberculosis Sanatoria in Panchgani and Wanlesswadi.

The class will be limited to 25 registered medical practitioners. Fifteen seats will be reserved for practi-

tioners in Western India, including Indian States, and the remaining for candidates from other parts of India.

Applications for the course in prescribed form should reach the Secretary, Tuberculosis Association of India, New Delhi, by the 22nd November, 1940.

The Tuberculosis Association also hope to organize a similar course in Calcutta early next year with the co-operation of the Bengal Tuberculosis Association. As soon as the preliminaries about this course are settled, a press note will be issued for general information.

#### KASAULI SANATORIUM SCHEME

1. Consequent on the transfer of the work connected with the manufacture and issue of anti-rabic treatment, the Association of the Pasteur Institute have offered



to place a major portion of their extensive estate measuring about 30 acres in area at the disposal of the Tuberculosis Association of India, free of cost, for the establishment of a Tuberculosis Sanatorium on such terms and conditions as may be mutually agreed upon.

2. The whole scheme for the establishment of the proposed sanatorium at Kasauli has been examined by an Advisory Committee appointed by Her Excellency the President of the Association and this Committee after careful examination of the proposals has approved the project and recommended that it be proceeded with subject to the receipt of certain grants which have been applied for.

3. The Sanatorium, when ready, will serve as a central institution for—

- (a) the modern treatment of pulmonary tuberculosis, especially difficult cases requiring advanced surgical treatment,
- (b) the training of doctors, nurses and health visitors in the modern methods of diagnosis and treatment of the disease, and
- (c) research work in tuberculosis including bacteriological research.

#### REVIEWS

(a) *Indian Red Cross Society, Mysore State Branch, Annual Report, 1939.*

During the year under report anti-tuberculosis work was carried on in the State under the auspices of the State Red Cross Branch. The nurses attached to the two solaria visited the houses of patients and the doctor in-charge checked their work and advised patients and their contacts. Contacts under 12 years of age who showed positive reactions to the tuberculosis test attended a solarium, where they were given graded sun-baths, cod-liver oil, fruit juice and milk. Anti-tuberculosis propaganda work was conducted by distribution of literature regarding infection and prevention.

(b) *Bengal Public Health Report for the year 1938.*

(i) The Director of Public Health, Bengal, writes that the increasing dust nuisance in the towns and even in the rural areas, on account of the increasing number of motor-cars and buses, has a direct repercussion on the incidence of respiratory diseases in general and pulmonary tuberculosis in particular. Hence arrangements should be made by the local bodies for the proper watering of the roads in towns and of putting a smoother surface on the roads, which will not produce dust.

(ii) The number of deaths in the province from pulmonary tuberculosis during the year under review was 14,668 giving a death rate of 0.29 per mille.

#### NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS, LONDON, NOTES

This Association has planned an interesting, enjoyable programme of health films, specially suitable for children. No mention is made of the word 'tuberculosis', but the children are taught the need of fresh air, the care of the teeth, cleanliness, etc. Teachers have expressed their whole-hearted approval of this programme.

#### ACTIVITIES OF INDIAN RESEARCH FUND ASSOCIATION

*Steps to improve Indian diets.*—Since it came into existence in 1911, the Indian Research Fund Association has devoted increasing attention to the study of nutritional problems and to the practical application of the fruits of such study to the improvement of the diet of the people, states the Report of Scientific Advisory Board of the Association for 1939. During the year under review, nutrition research has proceeded on the lines of surveys of the state of nutrition and the dietary habits of the people in various parts of the country, the analysis of the common foodstuffs of India for ascertaining their nutritional value, research into various nutritional problems, including that of

discovering cheap substitutes in order to meet recognized deficiencies in Indian diets, the training of health personnel in nutrition and educational work in order to encourage the application of the fruits of research for improving the diet of the people.

Rice, as the staple diet in many parts of India, received special attention during the year. A memoir entitled 'The Rice Problem in India', which deals with different aspects of the subject, has been recently published by the Indian Research Fund Association.

The results of over 50 diet surveys in different parts of the country have been embodied in a special publication by the Association and this should prove to be of value to provincial Departments of Agriculture in shaping agricultural policy in order to meet existing diet deficiencies.

#### TRAINING OF PERSONNEL

The training of health personnel in nutrition work, which was started in 1937, continued in 1939 and seventeen workers from various provinces and Indian States attended a three-months' course.

A new edition of *Health Bulletin No. 23*, entitled 'The Nutritive Value of Indian Foods and the Planning of Satisfactory Diets', was issued during the year and a nutrition museum was established at the Nutrition Research Laboratories at Coonoor, which is maintained by the Indian Research Fund Association.

Researches into different nutritional problems involved investigations in many centres, including medical colleges in Lucknow and Bombay, the Departments of Chemistry in Dacca and Calcutta Universities, the All-India Institute of Hygiene and Public Health, Calcutta, the Nutrition Research Laboratories, Coonoor, and the Imperial Agricultural Research Institute, New Delhi.

The Malaria Institute of India took a leading part in directing anti-malarial operations and research on scientific lines. The Director and other officers, through tours and by conferences with civil and railway health authorities, helped to place the expert services of the Institute at the disposal of these authorities for the solution of their malaria problems.

The annual class for training in malaria for medical officers from different parts of the country was carried out at Delhi by the Institute and 24 medical men attended this course. A considerable amount of laboratory research was carried out.

A new *Health Bulletin* entitled 'Lectures on Malaria' was prepared and a new edition of the practical entomological course for medical officers was published.

#### TRIALS OF PLAGUE SERUM

Plague research is mainly centred at the Haffkine Institute, Bombay. At the Cumbum Valley in Madras Presidency various field studies in regard to the control of epidemic outbreaks of the disease have also been in progress for the past eight or nine years.

At the Haffkine Institute research work on an anti-plague vaccine with maximum protective power was in progress. A serum for the treatment of plague patients had been prepared by this Institute and had undergone limited trials with encouraging results, during certain epidemic outbreaks of the disease.

At Cumbum Valley the research consisted mainly of work on the prevention of plague by the use of cyanogas for rat destruction in rat holes and by the reduction of rat infestation in houses through improved construction.

An investigation was carried out into the existence of varying degrees of disability among the population of certain areas in Madras Presidency as the result of high concentrations of fluorides in the drinking water supplies of these areas.

A considerable amount of research by field and laboratory studies into leprosy was in progress during the year. It has been shown that, in respect of chronic bone and nerve pain associated with leprosy, the adoption of a wheat diet by the patient affords him considerable relief. Another important finding is that the administration of skimmed milk to children with the

more severe forms of leprosy appears to help towards a cure.

The enquiries supported by grants from the Indian Research Fund Association covered a wide field including most of the major diseases affecting the health of the people of the country. A total sum of nearly Rs. 4,76,000 was distributed during 1939 in the form of grants to different enquiries conducted under the auspices of the Association.

### NUTRITIVE VALUE OF INDIAN FOODS

'APART from specific contributions to science, the Coonoor research unit has since its inception laboured to put nutrition on the map in India and to-day the importance of nutrition in relation to public health in India is generally realized' says the Note on the work of the Nutrition Research Laboratories, Coonoor.

Nutrition work in Coonoor has been financed throughout by the Indian Research Fund Association. The Raja of Parlakimedi, impressed by the importance of nutrition in India, made a donation in 1926 of one lac of rupees for nutrition research under Colonel McCarrison, the first Director of the Laboratories. This sum has been devoted to financing two research scholarships of the monthly value of Rs. 150 each.

### DIET SURVEYS

During the last five years great attention has been paid to diet surveys and up to the present time over 60 diet surveys have been carried out in various parts of India. The main object of diet surveys is to discover the defects of Indian diets and indicate the changes and improvements which are desirable from the standpoint of nutrition. A considerable number of points of importance in connection with agricultural and public health policy have emerged as the result of the surveys and these have been summarized in a note which has been circulated to agricultural departments.

### NUTRITION ADVISORY COMMITTEE

The Nutrition Advisory Committee is concerned with the development of nutrition work in India and includes as members the Public Health Commissioner, the Agricultural Commissioner and the Animal Husbandry Commissioner with the Government of India, the Director of the Nutrition Research Laboratories, some university professors of physiology and others with special interest in and knowledge of the subject.

### NUTRITION CLASSES AND PROPAGANDA

Since 1937 nutrition classes, lasting two to three months, have been held annually in Coonoor. Some 60 pupils from all over India have attended. Pupils are now employed as full-time nutrition officers in many provinces and states in India. Propaganda and educational work have been carried out by them in various parts of India and in general the scheme has resulted in the spread of knowledge of nutrition.

In addition to holding training classes and issue of popular bulletins, the Nutrition Research Laboratories deal with many requests for information which are received from all over India. Posters and other propaganda material are distributed to applicants, and from time to time popular lectures are delivered and press notes issued. There is no doubt that as a result of these efforts much progress has been made in spreading knowledge about diet in India in recent years.

### DRUG MANUFACTURE IN INDIA

'If essential raw and basic materials are available, the manufacturers in India could supply not only the whole of the normal requirements of the country in respect of medicines but would also be able to cater for export market' said Sir P. C. Ray, while presiding at the Second Annual General Meeting of the Indian Chemical Manufacturers' Association held on the 3rd

October, 1940, at Calcutta. As regards the heavy chemical industry, Sir P. C. Ray stated that many of the acids with few exceptions were being produced in this country. Some concerns had also started the production of alkalis, viz, soda ash, bleaching powder, caustic soda, etc., on a small scale and within a short period India would be producing these materials in sufficient quantity. Besides, several concerns have under project the manufacture of sodium and potassium bichromates, acetic acid, oxalic acid, tannic acid and other acids and alkalis. If, however, the stimulus provided by the war continued, the time would not be far off when, provided encouragement and support of the Government of India were available, this country would have a fully fledged chemical and pharmaceutical industry.

Sir P. C. Ray then referred to the question of co-ordination between the manufacturers and research institutions. In India, he said, several universities and other institutions were carrying on research on a number of items but there had not been much co-ordination so far between the institutions and the industry. He appealed to the research institutions as well as the manufacturers to put their heads together and suggested the establishment of a Chemical and Pharmaceutical Research Advisory Board consisting of representatives of the Indian Chemical Manufacturers' Association and of research institutions for exchanging views and advising the institutions about the subjects on which researches would be useful to the industry.

Coming to the handicaps under which the pharmaceutical industry in this country is labouring, Sir P. C. Ray stated that some of the provincial governments still hesitated and refused to implement the recommendations of the excise conference held in 1937. For instance, the Government of Bombay refused to reduce excise duty on spirituous medicinal preparations that might be used for other than medicinal purposes and toilet preparations and perfumes from Rs. 25-10 to Rs. 17-8. The Government of Sind also refused to reduce the excise duty on absolute alcohol and rectified spirit. He urged these governments to take steps to translate into action what they themselves approved at the excise conference, failing which he suggested that the Government of India, at whose initiative the conference met, should use their good offices to persuade these governments to implement the recommendations of the conference without delay.

The necessity of reducing high railway freight on raw drugs and medicines, which prevented the masses in India from getting cheaper medicines, was also emphasized. Coming to the activities of the Medical Stores Depôts, Sir P. C. Ray stated that although the requirements of the government in respect of medicines had considerably increased, the manufacturers were not benefited by the increase and the production of several items at the depôts was increased. There was no reason, according to him, why the manufacture of tinctures, spirituous preparations and extracts should be continued and extended at the depôts, when the drug industry was able to meet the normal requirements of the country both civil as well as military, the quality was reliable, and the prices were also cheaper.

While congratulating the Government of India for enacting the Drugs Act, 1940, Sir P. C. Ray regretted that the Government of India failed to appreciate the importance of having on the Drugs Technical Advisory Board representatives of the manufacturers. He also requested the Government of India to make arrangements with Indian States for enacting similar legislations or for adopting the Drugs Act, by the time the Act was enforced in British India.

### PRIZE ESSAYS

At a meeting of the subscribers of Sir Bhalchandra Krishna, Kt., memorial fund held on the 11th July, 1924, the following resolution was adopted:—

'That from the funds collected to perpetuate the memory of the late Sir Bhalchandra Krishna, Kt., a memorial prize medal be founded to be awarded every

year on the anniversary of his death to a member of the medical profession who submits a thesis or delivers a lecture on any medical subject before a meeting of the medical profession to be held under the auspices of the Bombay Medical Union, preference to be given to one who submits any original or research work especially with reference to indigenous medicine on western lines.'

In consonance with the above resolution, members of the profession are invited to submit a thesis or a paper by the 15th March, 1941, for submission to a selection committee for making the above award.

The thesis or paper will have to be read by the prizeman on the day of the award at a meeting of the profession to be held in accordance with the above resolution.

The following subject has been selected by the Bombay Medical Union for competitive thesis for the gold medal called the Dr. B. S. Shroff Memorial Gold Medal of the Bombay Medical Union for 1940:—

'The question of mortality in infants and children in India, laying special emphasis on measures to control it, and on detailed treatment of the various diseases causing it.'

The competitor must be (i) a duly qualified member of the medical profession holding a degree or degrees and diplomas from Indian and other Universities created by statute, or (ii) a duly qualified member of the medical profession holding the diploma of membership of College of Physicians and Surgeons of Bombay.

The thesis must be sent in six clear typed copies so as to reach the Honorary Secretaries, Bombay Medical Union, Blavatsky Lodge Building, French Bridge, Chowpatty, Bombay 7, on or before the 31st December, 1940.

The thesis should be designated by a motto instead of the writer's name and should be accompanied by a sealed cover containing the name of the writer and his post-office address. The name of the prize, the year of competition, the subject of the thesis, and the writer's motto should be superscribed on the cover.

No study or essay that has been published in the medical press or elsewhere will be considered eligible for the prize, and no contribution offered in one year will be accepted in any subsequent year unless it includes evidence of further work.

The accepted thesis shall be the property of the Bombay Medical Union.

All other theses shall be returned if not accepted provided the return postage expenses are paid in advance by the writer.

In the award of the prize to the successful candidate, the decision of the committee shall be final.

#### MEMBERS OF THE ACADEMIC COUNCIL OF THE DELHI UNIVERSITY

In pursuance of item (V) of sub-clause (1) of clause 5 of the First Statutes set out in the Schedule to the Delhi University Act, 1922 (VIII of 1922), His Excellency the Chancellor of the Delhi University is pleased to appoint the persons hereinafter named to be members of the Academic Council of the said University:—

Major-General G. G. Jolly, C.I.E., K.H.P., Director-General, Indian Medical Service.

#### ORDER OF ST. JOHN OF JERUSALEM

The King has been graciously pleased to sanction the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem:—

##### *As Knight*

Major-General Ernest William Charles Bradfield, C.I.E., O.B.E., K.H.S., I.M.S.

##### *As Officer (Brother)*

Colonel Thomas Crawford Boyd, M.R.C.P.I., F.R.C.S.I., D.P.H., I.M.S.

#### *As Serving Brother*

Lieut.-Colonel Robert Forrester Douglas MacGregor, M.C., M.B., M.R.C.P.E., I.M.S.

#### THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students are declared to have passed the L.T.M. Examination, Session 1940.

##### *Passed*

(Arranged in alphabetical order)

Musaddilal Aggarwal, L.M.F., junior honorary house surgeon, Chittaranjan Hospital, Calcutta.

Krishanlal Anand, L.S.M.F., private practitioner.

Satya Brata Bagchi, L.M.F., medical officer, Union Board Charitable Dispensary, Saidpur.

Rabindra Nath Banerjee, L.M.F., private practitioner.

Susanta Kumar Bhattacharjee, L.M.F., private practitioner.

Gobinda Chandra Bhattacharyya, L.M.F., house physician, Chittaranjan Hospital, Calcutta.

Hari Pada Chattopadhyaya, L.M.F., clinical assistant, Laboratory, S. K. Hospital, Mymensingh.

Bhupendra Kumar Chowdhury, L.M.F., private practitioner.

Ajit Kumar Das, L.M.F., private practitioner.

Sukhendra Kumar Das, L.M.F., private practitioner.

Hari Narayan Das Gupta, L.M.F., epidemic doctor, Darjeeling District Board.

Upendra Nath Das Gupta, L.M.F., private practitioner.

Gopal Chandra De, L.M.F., private practitioner.

Jyotirindra Nath Deb, L.M.F., private practitioner.

Debi Lal, L.M.P., sub-assistant surgeon, Victoria Hospital, Ajmere.

Prafulla Kumar Dora, L.M.P., honorary sub-assistant surgeon, Bargarh Dispensary.

Ganga Prasad, L.M.F., private practitioner.

Bimal Kumar Ghosh I, L.M.F., private practitioner.

Narendranath Ghosh, L.M.F., private practitioner.

Sukumar Ghosh, L.M.P., honorary physician, Purnea Hospital, Bihar.

Jodhraj Gupta, L.M.P., medical officer in-charge, Manglaur Dispensary, Saharanpur.

Sudhir Kumar Khastgir, L.M.F., private practitioner.

Baij Nath Khanna, L.M.F., private practitioner.

Dattatray Balvant Kothari, L.M.P., private practitioner.

Amitabha Maitra, L.M.F., house surgeon, Sadar Hospital, Berhampore.

Sasanka Shekhar Majumdar, L.M.F., sub-assistant surgeon, B. N. Ry.

Hari Narhar Mandke, L.M.P., private practitioner.

Sarat Chandra Misra, L.M.P., sub-assistant surgeon, Government of Orissa.

Mohammad Shamsazzoha Pramanik, L.M.F., assistant medical officer, Dalmore Tea Estate Dispensary and Hospital, Jalpaiguri.

Lalit Chandra Mojumder, L.M.F., assistant medical officer, Toorsa Tea Estate, Jalpaiguri.

Aratrik Ranjan Mukerjee, L.M.P., private practitioner.

Abani Bilas Mukherjee, L.M.P., private practitioner.

Kishori Prosad Mukherji, L.M.F., private practitioner.

Radhey Behari Nigam, L.M.P., L.C.P.S., private practitioner.

Sakharam Shivalingappa Panade, L.C.P.S., L.G.O. (Madras), S.M.S., Government of Bombay.

Vitthalbhai Ramdas Patel, L.C.P.S., private practitioner.

Jyotish Chandra Paul, L.M.F., private practitioner.

Promode Ranjan Paul, M.B., assistant medical officer, Anglo-India Jute Mills, Jagatdal.

Kaduvam Sheetharamiengar Ramaswami, L.M.F., private practitioner.

Thakorbbhai Dahyabhai Rana, L.C.P.S., private practitioner.

Samuel Richard, L.M.P., private practitioner.

Indu Bhusan Roy, L.M.P., private practitioner.

Suresh Chandra Saha, L.M.F., private practitioner.

Amar Prasad Sarkar, L.M.F., private practitioner.  
 Dharendra Chandra Sen, L.M.F., assistant medical officer, Kamarbund Tea Estate, Assam.  
 Ardendu Bhusan Sen Gupta, L.M.F., private practitioner.  
 Amritlal Prabhasanker Shukla, L.C.P.S., private practitioner.  
 Channan Lal Talwar, L.M.F., private practitioner.  
 Arvindkumar Mohanlal Vakharia, L.M.P., private practitioner.

## CORRIGENDUM

## REPORT OF AN ENDOCRINE CLINIC: SPACKMAN

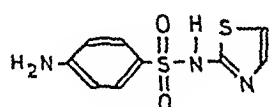
In the above paper which appeared in our September issue, p. 555, under the heading *Disorders of lactation*, 2nd paragraph, the last three lines read 'The effect is not impressive and begins within 24 hours, the injections occasionally are rather painful' should read 'The effect is most impressive and begins within 24 hours; the injections occasionally are rather painful'. The mistake originated through a typing error in the author's typescript.

## Current Topics

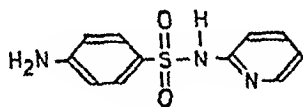
## Sulphathiazole

(From *The Lancet*, Vol. I, 11th May, 1940, p. 883)

It has been freely predicted that the successes of sulphanilamide and sulphapyridine in the treatment of bacterial infections would lead to therapeutic claims for other similar compounds which the chemists can readily prepare. Such a compound is 2-(para-amino-benzene-sulphonamido) thiazole, a preparation in which sulphanilamide is linked to thiazole, a heterocyclic compound, in the same way as it is linked with pyridine in sulphapyridine.



Sulphathiazole.



Sulphapyridine.

This preparation, provisionally called sulphathiazole, and its 4-methyl derivative (sulphamethylthiazole) have been distributed in America for experimental and clinical trial, although not yet released in the open market. Early tests suggested that sulphathiazole and

... more effective than sulphapyridine in the treatment of bacterial infections, and Helmholz has lately shown that *in vitro* the urine of patients receiving these drugs is bactericidal for both *Staphylococcus aureus* and *Streptococcus faecalis*. Another report from the Mayo Clinic on the results obtained with these two preparations in urinary infections caused by coliform bacilli (15 cases), *Streptococcus faecalis* (7 cases) and *Staphylococcus aureus* (5 cases) claims a 65 per cent cure rate. These results naturally prompt us to ask how these new drugs compare in activity and toxicity with those already in use for the treatment of bacterial infections. Perrin Long has presented a report to the American Council on Pharmacy and Chemistry which summarizes the available American data on these two points. It seems that in experimental pneumococcal infections the new drugs are rather less effective than sulphapyridine, in streptococcal infections they are about equal, and in staphylococcal infections (which are more difficult to assess) they are somewhat superior to sulphapyridine. Clinical data from America on the treatment of infections due to these bacteria are, with the possible exception of staphylococcal infections, still too scanty to allow an opinion on the usefulness of these preparations. However, a similar product, called Ciba 3714, has been clinically tested, in doses similar to those adopted for sulphapyridine, in a variety of bacterial infections by Gsell. Among 60 patients with pneumonia, of whom 23 had lobar pneumonia and the others bronchopneumonia and post-influenzal pneumonia, there was in general a rapid amelioration of symptoms and only 1 death, while 7 cases of acute cerebrospinal fever

all recovered. The concentration of the drug in the cerebrospinal fluid was 4-6 mg. per cent, some 50-60 per cent of the blood level. Cases of gonorrhoea, erysipelas, and coliform pyelitis and cystitis were also treated with success but 2 cases of generalized staphylococcal infection failed to respond. Staphylococcal infections are indeed likely to be a stumbling-block for ... : cause of their great tendency to form ... . If it is to be effective the drug must be given very early, for without surgical drainage it has little chance of success once pus has accumulated.

As regards its pharmacology and toxicity, sulphathiazole is readily absorbed from the bowel and quickly excreted, while a smaller percentage of the drug becomes acetylated and inert than is the case with sulphapyridine, although experience with the latter drug shows that ... conjugated drug varies greatly in ... . With doses of 4 to 6 g. of sulphathiazole per day the concentration in the blood seems to range between 3 and 5 mg. per cent (the Swiss workers claim higher levels), and higher concentrations are difficult to maintain despite increases in the amount of drug prescribed. This is presumably due to the rapid excretion of the drug, and may be a point of some practical importance, especially in severe infections. Experimentally in mice the chronic toxicity of sulphathiazole is greater than that of sulphapyridine, while the sodium salt of the methyl derivative is as acutely toxic as the corresponding salt of sulphapyridine. In man, nausea and vomiting are less common than with sulphapyridine, and according to both the Swiss and American investigators are never severe enough to interfere with the use of the drug, even with doses of 8-12 g. per day. If confirmed, this is a point definitely in its favour. Drug rashes and drug fever are quite common, and some patients have shown an acute congestion of conjunctiva and sclera in association with a rash resembling that of erythema nodosum. Haematuria has been noted in several cases, and is more likely to occur with sulphamethylthiazole which is poorly soluble. In other words, the toxic effects are much the same as those produced by sulphapyridine except that the latter drug is more liable to cause vomiting.

The position with regard to the new preparations is admirably summed up by Lond: 'The evaluation of these new chemotherapeutic compounds', he says, 'will necessitate extensive experimental and clinical investigations in order to determine their efficiency in the control of infections and their clinical toxic manifestations. Until the time when such data are in hand, it is to be hoped that enthusiasms do not outrun common sense'.

[In *The Lancet*, i, 18th May, 1940, p. 946, a correspondent (W. R. Throver) pointed out that sulphathiazole was prepared in the laboratories of May and Baker early in 1938. They found it less effective against pneumococcal infections than M. & B. 693, but are now re-investigating its anti-staphylococcal value.]

## Comparative Effects of Phenobarbital and Dilantin Sodium in the Treatment of Epilepsy

By L. J. ROBINSON, M.D.

and

R. OSGOOD, M.D.

(From the *Journal of the American Medical Association*, Vol. CXIV, 6th April, 1940, p. 1334)

MATERIAL for this study comprised a group of 100 patients at the Monson State Hospital, who were selected on the basis of frequency and regularity of convulsive attacks regardless of diagnosis, age, sex, age of onset, duration of attacks, mental status, physical condition or previous medication. The vast majority of patients had been having ten or more seizures per month regularly. Medication previous to this study had consisted of phenobarbital in doses of 3 grains (0.2 gm.) or less daily.

The effect of treatment by phenobarbital or dilantin sodium was evaluated on the basis of effect on seizures, salutary effects, effects on the general condition of the patient, and untoward effects. The therapeutic response was graded as follows:—

Group 1. Complete control of, or marked reduction in, the number of seizures, with absence of untoward effects or only slight and easily managed untoward effects.

Group 2. Moderate reduction in the number of seizures with salutary effects or easily controlled untoward effects.

Group 3. No appreciable reduction in the number of seizures or increased number of seizures, with or without untoward effects; or marked untoward effects which could be managed only by terminating treatment and which overshadowed any anticonvulsant and/or salutary effects.

Group 4. Indeterminate, no definite favourable or unfavourable effects being noted during the period of observation.

Our study divided itself into the following three phases: (1) treatment with phenobarbital alone, (2) treatment with dilantin sodium alone and (3) treatment with a combination of phenobarbital and dilantin sodium.

### PHENOBARBITAL IN EPILEPSY

The 100 patients, representing the total number of cases included in our complete study, were given phenobarbital in gradually increasing doses either until the optimal anticonvulsant effect was obtained or until untoward effects contra-indicated further increases or demanded reduction in dosage. Thirty-seven of the 100 patients derived marked benefit from the larger doses of phenobarbital alone and are classed as P 1 (P refers to phenobarbital and the numeral 1 to group 1 in the classification previously indicated). During the period of increased phenobarbital dosage, the maximal and optimal doses of phenobarbital ranged from  $3\frac{1}{2}$  to  $11\frac{1}{2}$  grains (0.2 to 0.7 gm.) a day. Twenty-eight patients are taking 6 grains (0.4 gm.) or more of phenobarbital a day and twelve are receiving 9 grains (0.6 gm.) or more of phenobarbital a day. Twenty-seven of the thirty-seven patients have been on the larger doses of phenobarbital for from eleven to fifteen months and ten for from three to ten months. Only a few patients experienced untoward effects, which have been slight, transient and easily managed. Salutary effects have been common, consisting of increased activity, alertness, desire and willingness to work, and greater interest in surroundings.

### DILANTIN SODIUM IN EPILEPSY

Fifty-six patients who were not greatly benefited by large doses of phenobarbital were given dilantin sodium in gradually increasing doses, ranging from 3 to  $13\frac{1}{2}$  grains (0.2 to 0.9 gm., or two to nine capsules). The criteria used for changing medication from phenobarbital to dilantin sodium were (1) complete failure of large doses of phenobarbital to lessen frequency of

seizures, (2) only slight to moderate reduction in the number of seizures and (3) untoward effects associated with large doses of phenobarbital, which either prevented raising phenobarbital to the anticonvulsant level or which overshadowed any favourable anticonvulsant effects.

Forty-five of the fifty-six patients have been followed for from two to eight and one-half months while taking dilantin sodium and eleven for from three weeks to two months. The length of time these patients had been receiving the larger doses of phenobarbital varied from three weeks to six and one-half months.

Evaluation of the results obtained with this group of patients is summarized as follows:—

Twelve, or 21.4 per cent, obtained excellent improvement on dilantin sodium with regard to both anticonvulsant and salutary effects (group 1). Of these twelve patients only two did equally well on phenobarbital.

Seventeen patients, or 30.3 per cent, showed moderate improvement on dilantin sodium (group 2). Of these seventeen patients, eleven did equally well on phenobarbital and six were definitely worse on phenobarbital.

Totalling the number of patients in groups 1 and 2, we find that twenty-nine, or 51.7 per cent, were much improved on dilantin sodium. This includes thirteen patients who did as well on phenobarbital.

Twenty-seven patients, or 48.2 per cent, did poorly on dilantin sodium (group 3). Of these twenty-seven patients, four did moderately well on phenobarbital, and twenty-three did as poorly on phenobarbital.

Whatever results have been obtained with dilantin sodium have been obtained in a group of patients all but two of whom were selected on the basis of failure to respond satisfactorily to large doses of phenobarbital. The results with dilantin sodium impress us as especially significant because we are inclined to believe that any anticonvulsant drug is unlikely to show up to its best advantage in many institutional patients of this type.

There was no correlation between results with dilantin sodium and dosage, for some patients taking as little as  $4\frac{1}{2}$  grains (0.3 gm. or three capsules) of dilantin sodium did very well, while others receiving as much as  $13\frac{1}{2}$  grains (nine capsules) did not do well. The optimal dose varied from 3 to  $10\frac{1}{2}$  grains (0.2 to 0.7 gm., or two to seven capsules). Likewise there was no correlation between the size of the dose of phenobarbital and the results obtained. The optimal dose of phenobarbital varied between 3 and 11 grains.

While, to be sure, most patients in this series experienced toxic effects from the larger doses of phenobarbital or from dilantin sodium at some time, it should be kept in mind that, in the very nature of this investigation, unless an appreciable anticonvulsant effect was produced by a non-toxic dose, it was necessary to increase medication steadily to the point of toxicity.

Lethargy, ataxia, anorexia, nystagmus and tremor were toxic effects common to phenobarbital and dilantin sodium; whereas epigastric distress, ocular pain, diplopia and hyperplasia of the gums were related solely to dilantin sodium. Benzedrine sulphate was found effective in controlling apathy and lethargy, and sodium bicarbonate in controlling nausea and vomiting. The other untoward effects were controlled by decreasing the dose of the drug. A distinct advantage of dilantin sodium is the lack of sedative effects except in toxic doses, which is in marked contrast to the effects of phenobarbital in the larger therapeutic doses. None of our patients had dermatitis while on dilantin sodium, and no serious untoward effects were associated with dilantin sodium therapy.

From experience gained during the course of this study, we believe that untoward effects could often have been considerably lessened had we increased the doses of phenobarbital and dilantin sodium more slowly than was done and temporarily reduced the doses more often during periods of inactivity. During the first part of the period in which we used dilantin sodium we gave some patients as much as nine capsules a day ( $13\frac{1}{2}$  grains), since we did not know what the limit of dosage should be. Untoward effects were common and almost invariable when more than six capsules



Can bend knees to about 90 degrees and stretch them out. Can sit up alone, using his arms to help. Wheels himself in chair with comfort.

*Case 9.*—Male, aged 14. Advanced case. Could not walk, chiefly due to contractures of legs. Arms very weak. Could just use wheeled chair. Could not get into bath. Full sexual development. After five months' treatment he wheels himself about in his chair freely. All muscles in arms much stronger. Can get into bath.

*Case 10.*—Male, aged 9. Early case. Younger brother affected. Getting worse in spite of massage for last year. Stumbled often when running. Stairs difficult. Calves typical. After three months' treatment and massage calves much softer. He appears better to me, though his mother is dubious.

*Case 11.*—Male, aged 22. Advanced case. Great weakness of arms and shoulder girdle. Contractures of thighs. Leg muscles not greatly affected. Normal sexual development. After nine weeks' treatment legs stronger, arms very much stronger. For the next four months treatment was stopped, and both arms and legs were much weaker.

*Case 12.*—Male, aged 8. Early case. Slight improvement in walking reported in a month.

*Case 13.*—Male, aged 30. Advanced case. Condition first noticed nineteen years ago. Hardly any change in last three years. Can just stand and just shave. Sexual development normal. No effect from six weeks' treatment.

*Case 14.*—Male, aged 14. Advanced case. Mentally deficient. Full sexual development. No change with four months' treatment.

*Case 15.*—Male, aged 10. Advanced case. Bed-ridden. Treatment and massage had no effect in a month.

*Case 16.*—Male, aged 18. Very advanced case. Gross wasting of all muscles. Could not move or feed himself. Sexual development normal. Six weeks' treatment had no effect.

*Case 17.*—Male, aged 17. Advanced case. Bed-ridden. Could just feed himself. Sexual development normal. Six weeks' treatment had no effect.

*Case 18.*—Male, aged 10. Very last stages. Died after a month's treatment.

#### AMYOTROPHIC LATERAL SCLEROSIS

*Case 19.*—Male, aged 49. Six years ago whole of right hand suddenly became numb and paralysed, with great wasting. Arm not affected. Apparently diagnosed as brachial neuritis. Right hand has slowly improved since. Six months ago left hand started to feel weak and to waste and legs felt tired, the condition slowly getting worse. Amyotrophic lateral sclerosis was diagnosed by a consulting physician and his own doctor. On examination he appeared to be a typical case. There was gross wasting of all muscles of the right hand. The left hand had some wasting of the thenar muscles and the interossei but no fibrillation. There was extensive fibrillation of all the muscles of both legs and feet. All reflexes were normal. There were no sensory changes. Two months after beginning treatment there was no longer any feeling of tiredness in his legs, and his hands if anything were stronger. The left thenar muscles appeared less wasted. Fibrillation was worse in the legs. A month later there was definitely more muscle both in the left hand and the right, and the fibrillation in the legs had decreased. After seven months' treatment, 'he has forgotten his left hand was ever weak'. His legs feel normal. On examination his left hand appears normal, his right much stronger and with an increase in muscle. There was no fibrillation in his right leg or foot, and very little in his left.

*Case 20.*—Female, aged 65. Six months' history of progressive weakness and stiffness of legs and weak hands. On examination could just walk across room. Legs spastic, extensor response mild fibrillation. Hands slightly wasted, worse after a month's rather

uncertain treatment; but after another two months' treatment is reported to be improving.

*Case 21.*—Female, aged 45. Treatment was started in the last stages of bulbar paralysis, and the patient died six weeks later.

*Case 22.*—Female, aged 38. Treatment was started in the last stages of bulbar paralysis, and the patient died four weeks later.

#### TABES DORSALIS

*Cases 23 and 24.*—Two cases of tabes dorsalis, one blind and both bed-ridden, were treated for eight weeks for very severe lightning pains and abdominal crises. Neither improved.

#### PERONEAL MUSCULAR ATROPHY

*Case 25.*—Male, aged 18. His maternal uncle died of peroneal muscular atrophy. The patient developed symptoms when he was 12, which have progressed very slowly, neither hands nor feet being very affected. His sexual development is normal. Two months' treatment has had no effect. The progress of the disease is too slow to know if it has been checked or can be improved.

#### AMYOTONIA CONGENITA

*Case 26.*—Female, aged 2½. There had been extreme muscular weakness since birth. The child could just raise her arms and draw up her legs but could not roll over or raise her head. There was gross kyphosis. After three months' treatment and massage she could kick her legs in the air and her arms were much stronger. She could raise her head and could roll over. Vitamin E was then stopped, and her improvement appeared to be slower.

#### DISCUSSION

In the group of the myopathies—chiefly children—the results of treatment with vitamin E were remarkable. Every patient improved who was treated for more than six weeks, except case 14, who was mentally deficient. When it is remembered that these cases should have got worse or at least remained the same, such definite improvement in 12 cases out of 13 must mean that this treatment promises success in a disease which has always, until now, been hopeless. The slowness, however, of the recovery and therefore the necessity for prolonged treatment must be emphasized. Recovery has continued in case 1 for eighteen months and in no case has shown any signs of stopping. How far it can go is as yet unknown, but there seems to be no reason why patients in an early stage should not recover completely provided that they continue to be treated. The diagnosis, however, should be definite before treatment is begun; otherwise an apparently normal child may continue to be treated to guard against a relapse of a disease he may never have had. This danger of a relapse is shown in case 11.

Even bed-ridden patients show improvement. Since these children often have a long period of growth still before them, it seems possible that they may recover enough to lead comparatively normal lives. Since much of the disability in advanced cases may be due to contractures, these should be dealt with surgically at the beginning of treatment so that the recovering muscles can function normally.

No ill effects or sexual stimulation have been seen during treatment.

Not enough patients with amyotrophic lateral sclerosis have been treated for the results to be definite, but on the whole I think they are promising. Case 19, in whom the disease is arrested and who feels normal again, has no obvious involvement of upper neurones. Case 20 has been treated for three months, and is reported to be improving. The two patients who died had advanced bulbar involvement before treatment began.

The two cases of tabes (23 and 24) were too advanced for the negative results to be of any value, but I still believe vitamin E will be found of value in this condition. The man with peroneal muscular atrophy



(case 25) has not been treated long enough for any conclusions to be drawn. The small girl with amyotonia congenita (case 26) appeared to have been greatly improved.

It appears reasonable to suggest that in all degenerations of the muscular or nervous systems, such as disseminated sclerosis, a large supply of vitamin E should be of value; for, though a deficiency may not be the cause, yet a sick cell should have an abundance of what is necessary for its life. It also may be that in children who have a diet rich in vitamin E the anterior-horn cells would be more resistant to infantile paralysis; hence, at least during epidemics, the vitamin should be used as a protection.

The clinical results reported here strongly confirm the deductions which Einarson and Ringsted made from their laboratory work. The discovery of the importance of vitamin E in the treatment of muscular and nervous diseases appears to be revolutionary. It opens up new lines of thought and treatment in many diseases. It appears indeed to be one of the great advances in general medicine of the century.

#### SUMMARY

The laboratory work of Einarson and Ringsted is discussed, and the reasons are given for their suggestion that the muscular dystrophies, amyotrophic lateral sclerosis, and tabes dorsalis are deficiency diseases due to lack of vitamin E.

Normal human diets may be poor in vitamin E.

The results of giving vitamin E for muscular dystrophy and amyotrophic lateral sclerosis support the contention that these are deficiency diseases and curable.

### Medical Aspects of the Use of Food

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THE medical aspects of the use of food are manifold, and include such matters as food allergy, food poisoning, microbic and parasitic agents conveyed to man in food, and the treatment of disease by food. I shall confine myself to the relation of food as a whole to the preservation of health, the constituents of a properly constituted diet, the relation of such constituents to the structure and functions of the living body, and the effects of the inadequate supply or utilization of these essentials in causing disease.

Food may be defined as anything which when taken into the alimentary tract provides, on digestion, materials for the energy requirements, growth, maintenance, repair, and regulation of the vital activities of the body. The materials are many: proteins, fats, carbohydrates, minerals, vitamins, pigments, blood-forming substances, extractives, and flavouring matters. The food must also contain a certain amount of roughage to stimulate intestinal movements, and there is something, again, in the freshness of food which gives it a health-promoting influence. No single food-stuff contains all these properties. Even milk, which is the nearest approach to a complete food, lacks one and may lack more of them. A properly constituted diet is such a combination as contains them all in proper quantity and proportion.

#### NATURAL FOODSTUFFS

In order to learn what a properly constituted diet is we may consider the diet of the peoples of India, as it was among them that most of my own work was done. With the exception of the races whose staple article of food is rice—the nutritive value of which is usually debased by various treatments before use—the Indian peoples have national diets composed of the unsophisticated foodstuffs which their fields and pastures provide. Some of the peoples of Northern India are unsurpassed for perfection of physique, powers of endurance, and resistance to disease. Others,

particularly the rice-eating races of the west and south, are of poor physique, low powers of endurance, and subject to much disease. Maladies such as tuberculosis, leprosy, dysentery, and many others are more common in the south and east than in the north. McCay came to the conclusion that food was the all-important determining influence, and the conclusion has been confirmed by the results of my own experiments.

The best diet was found to be one similar to that used by certain hardy, agile, vigorous races of Northern India—a diet composed of freshly ground whole-wheat flour made into cakes of unleavened bread, milk, butter, pulses, fresh green leaf and root vegetables, and fruit, with meat occasionally. Many other experiments were made which showed that when previously healthy animals were fed on improperly constituted diets, such as are habitually used by human beings, they developed many of the diseases from which these human beings tend to suffer—diseases of the bony framework of the body, of the skin and membranes, of the glands, of the gastro-intestinal tract, of the lungs, of the nerves. All these were produced in animals under experimental conditions by feeding them on faulty human diets.

A properly constituted diet is one made up of whole cereal grains, milk and its products, pulses, green leaf and root vegetables, fruit, with eggs or meat, or both, on occasion. The dependence of health on a diet composed of these natural foodstuffs or others of like nutritive value is the essence of the whole matter of food in relation to health and of food deficiency in relation to disease. It relieves the layman, or for that matter the doctor, of all or nearly all anxiety as to whether the food contains this or that constituent. It provides both for essential constituents of food already known and for those not yet known. There is, however, this proviso—that the foodstuffs must be produced on soils that are not themselves lacking in essential mineral and other substances, nor themselves rich in substances harmful to the body. Another proviso is that, owing to lack of sunshine at certain seasons of the year in this country, and to the sparse distribution of vitamin D among foodstuffs, it is necessary to add cod-liver oil or halibut-liver oil to the list given above.

For many years it was thought that proteins, minerals, fats, and carbohydrates sufficed for the growth, maintenance, repair, and energy requirements of the body. It is now known they do not suffice, and with new analysis and methods of investigation many other essential constituents of food have been found. Nevertheless, this older knowledge showed the fundamental relations of energy-yielding constituents to vital processes, also the importance of the protein factor in nutrition, and this older knowledge still stands.

#### THE VITAMINS

For some years following the discovery of vitamins and of their deficiency in the food as the cause of the maladies now known as the deficiency diseases, certain limiting terms—anti-this and anti-that—were attached to them. But further research showed that they had much else to do besides the prevention of these diseases. It is this 'much else' that concerns us, for these maladies result from the complete or almost complete absence of the respective vitamins from the food, a contingency rarely met with in this country. It is not with complete but with partial deficiency that we are chiefly concerned. This partial deficiency is relatively common, certainly among the poorer classes, and it is becoming generally recognized that much sub-normal health and development and even incidence of disease are associated with it.

It is well, therefore, to have a working knowledge of the functions of the more important vitamins and minerals and of the effects on the body of their insufficient supply or utilization. For just as the knowledgeable gardener knows when his plants are not thriving for want of some nutrient, so should the knowledgeable parent know when her children are not thriving for the same reason. It is extraordinary how quickly one's powers of observation grow in this respect. I find myself saying of this or that child or

young person: You need lime, you iron, you vitamin B<sub>1</sub>, you vitamin A, you vitamin C, and you all of them.

*Vitamin A* is essential to growth and development of the young. It maintains the normal structure of mucous membranes, protecting them against infection. It controls the content of visual purple in the retina and has important relations to the enamel-forming organs of the teeth and to the structure of the blood, bone marrow, certain glands, and the nervous system. Its deficiency gives rise to poor growth of the body, eye affections, night blindness, dry or scaly skin, enamel-poor teeth, and to inflammatory states of mucous or other membranes. Rich sources of the pre-formed vitamin are animal fats, cod-liver oil, milk, butter, cream, liver, egg, and herring. Rich sources of its precursor—carotene—from which it is formed in the body itself, are carrots and fresh green vegetables.

*Vitamin B* is a complex of many vitamins. Vitamin B<sub>1</sub>—now known as aneurin or thiamin—is necessary for the structural and functional efficiency of the nervous system; consequently its adequate supply is essential to all neuro-muscular activities, including those of the heart, the stomach, and the bowels. The structural and functional efficiency of the adrenal gland depends largely upon it. It is related in a specific way to carbohydrate metabolism and is essential to growth. When absent from or very deficient in the diet the disease known as beri-beri arises. Its insufficient consumption or utilization may give rise to anorexia, poor growth, lack of vigour, fretfulness or nervousness, cardiac and bowel irregularities, and neuritis. The chief sources of vitamin B<sub>1</sub> are yeast, marmite, whole cereal grains, egg yolk, liver, fresh green vegetables, and tomatoes. The body, in the course of its chemical activities, uses up the vitamin and does not store it to any extent; its constant and liberal replacement is therefore necessary. The chief cause of its insufficiency in the diets of our people is the almost universal use of white flour, from which it is lacking, in preference to whole-meal flour, in which it is abundantly present, and the excessive consumption of vitaminless sugar.

The other fractions of the vitamin B complex may be grouped together. Their functions include the activation of combustion processes, the promotion of growth, blood-forming activities, and a very important contribution to the maintenance of health of the skin, the mucous membranes, the gastro-intestinal tract, liver, heart, nervous system, and mind. One or more fractions are concerned in preventing pellagra; another appears to have something to do with the prevention of cataract; and a third has blood-forming functions. Deficiency may give rise to buccal, lingual, and gastro-intestinal ailments and to anæmia. The chief sources of the complex are yeast, liver, kidney, muscle meat, egg, milk, and green vegetables.

*Vitamin C* (ascorbic acid) has an important part to play in the chemistry of oxidation-reduction processes. It maintains the structural integrity of the cement substance which holds the cells of the body together. Consequently it has a close concern with the structural integrity of the capillaries, bones, teeth, gastro-intestinal tract, and mucous membranes. Its absence from the diet gives rise to scurvy. Its insufficient supply may cause hæmorrhage into, or easy bruising of, exposed parts of the body, sallowness and unhealthiness of the skin, imperfections of the teeth, fragile bones, unhealthy gums, and gastro-intestinal disorder. Rich sources of the vitamin are parsley, chillies, orange and lemon juice, green leaf vegetables, and potatoes.

*Vitamin D* (calciferol) controls the absorption and utilization of calcium and phosphorus. Its adequate supply is therefore of the utmost importance to the normal structure of the bones and teeth. Its deficiency gives rise to rickets, dental disease, and to slow healing of fractures. It is sparsely distributed among foodstuffs, occurring in considerable quantities only in fish oils, egg, liver, milk, and butter, and therefore it is deficient in the diet of many people.

*Vitamin E* is the so-called 'anti-sterility vitamin', but it has other relations besides those to reproduction.

It is indispensable to growth and to bodily functions generally. Research tends to connect it with the pituitary body, that master-gland of the endocrine system. Its chief source is wheat-germ oil.

The other vitamins I must pass by with the general remark that between them they contribute a considerable share to the health of the skin, the efficiency of the functions of reproduction and lactation, the maintenance of the normal composition of the blood, the prevention of hæmorrhage, and the promotion of growth.

#### MINERAL CONSTITUENTS

The mineral constituents of food consist of some twenty elements, of which eleven are known to be essential to vital processes. In general their functions are to provide building materials for the fabric of the body and to regulate various functions. Some enter into the composition of all cells; others form the major part of the skeleton and teeth. In fulfilment of their regulating functions they have various parts to play: all are concerned in controlling the normal exchanges of body fluids and the permeability of the cell membranes; some maintain and regulate the neutrality of the blood, others the normal contractility of the muscles and excitability of the nerves; some enter into the composition of the digestive juices, others take part in the transport of oxygen from the lungs to the tissues and of carbon dioxide from the tissues to the lungs, thus making oxidation process possible. Indeed, the more the mineral constituents of food are studied the more important is their rôle in nutrition found to be.

From the point of view of dietary construction four of these mineral elements—calcium, phosphorus, iron, and iodine—are of outstanding importance, not only because of their own functions but because they are those most likely to be present in the average diet in insufficient quantities. In the diet the amounts of these minerals should be adjusted with the same care as is given to those of proteins, carbohydrates, fats, and vitamins, and in estimating the quantities of essential components in any diet the calculations should always include these four elements. By making provision for their ample supply no serious deficiency of any other mineral essential is likely to arise.

*Calcium* is a chief constituent of the bones and teeth. It controls the contractility of muscle, and the rhythmic beat of the heart depends to a great extent upon it. It maintains the normal response of the nerves to stimuli, preventing their hyper-irritability, preserves the clotting power of the blood, and sustains the capillary circulation. Calcium is made use of in the body to the extent of about 0.68 gramme daily, but to allow a fair margin the food should provide at least one gramme a day, and even more for expectant mothers and growing children. The insufficient supply of calcium is one of the commonest of all food faults in this country. It is difficult for the growing child under modern conditions to obtain enough calcium unless the diet contains at least a pint of milk a day. The diet of pregnant women is often dangerously low in calcium. Recent researches in America have shown that such women need 1.6 grammes daily; often they do not receive one-half of this amount. Deficiency leads, in growing children, to imperfect building of bones and teeth, to rickets and all its attendant consequences, and to malformation or mal-alignment of the vertebræ. Not infrequently the normal calcium content of the blood, on which so many bodily activities rely, is being maintained at the expense of decalcification elsewhere—of teeth, alveoli, and bones. Want of calcium leads also to nervous excitability and to tetany, to impaired muscular activity, and to disturbance of cardiac rhythm and of the neutrality of the blood. Foods rich in calcium are (weight for weight and in descending order of richness) cheese, turnip-top greens, black treacle, almonds, water-cress, dried figs, egg yolk, milk, beans, lentils, oatmeal, turnips, whole wheat, and green leafy vegetables.

*Phosphorus* is an essential component of the nuclei of all cells, and therefore plays a conspicuous part in

all cellular activities. It should be provided in the diet to the extent of 1.5 grammes daily, and increased during pregnancy. Deficiency may lead to stunting of growth, poor bone formation, softening of bone, a type of rickets, tooth decay, disturbance of neutrality of blood, and depression of vital processes generally. Foods rich in phosphorus are cheese, egg yolk, oatmeal, lean meat, chocolate, almonds, nuts, dried peas and beans, whole wheat, liver, milk, fresh beans, spinach, brussels sprouts, currants, raisins, and potatoes.

*Iron* is also concerned in the control of all cellular activities. It is a component of haemoglobin, the carrier of oxygen from the lungs to the tissue cells. The diet should contain at least 15 milligrammes of iron daily, increased to 20 during pregnancy. It is estimated that the iron content of the average diet in England is rarely more than 100 milligrammes, frequently as low as 5. In these circumstances anaemia is likely to arise. Foods rich in iron are lentils, egg yolk, liver, dried peas and beans, black treacle, oatmeal, whole wheat, dried currants, almonds, turnip-top greens, spinach, dried prunes, dates, figs, and raisins.

*Iodine* is an essential constituent of the thyroid gland and of its active principle, thyroxine. In normal circumstances the daily requirements of iodine are about one-thousandth of a milligramme. Growing children and pregnant and lactating women need more of it than others. Its deficiency or inadequate absorption or utilization gives rise to goitre and its tragic sequel, cretinism, in which bodily and mental development is gravely retarded. Foods rich in iodine are sea foods, cod-liver oil, eggs, goat's milk, fresh vegetables, and some condiments.

#### THE FUNCTION OF PROTEINS

Apart from water, proteins are the most abundant constituents of living cells. Their chief rôle in the body is to provide materials for its growth and for the repair of its tissues. Their continuous supply is, therefore, necessary, and this supply must be of the right kind, to furnish the requisite amino-acids, derivatives of proteins, from which the various tissues are built up. Besides their function as providers of building materials they also furnish a certain amount of energy. They are the source from which the body elaborates some enzymes for ferments, such as those concerned in the digestive processes, and catalytic agents needed for the speeding up of chemical processes.

The daily requirement of the body for proteins is approximately one gramme per kilogramme of normal body weight. More than this is an undesirable excess. Sources of them among animal foods are milk, meat, glandular organs, eggs, and fish; and among vegetable foods, legumes, whole cereal grains, seeds, nuts, and green vegetables. Those derived from animal sources are, in general, more suited to the needs of the human body than those derived from vegetable, but it is not necessary that the protein requirements of the body should be derived mainly from animal sources; it is sufficient if one-third is so derived. Nor is it necessary that 'good' proteins as distinct from second-class should be derived from meat. Those of milk are among the best of all proteins and well able to leaven the whole lump of those derived from vegetable foods. For this reason, among others, the use of milk and cheese as articles of diet should be greatly extended. Much greater use should also be made of the better-class vegetable proteins, such as those of the soya bean and whole wheat, and much less use of the flesh of animals. Apart from every other consideration, the use of meat as the main source of proteins is as uneconomical as it is unnecessary—but where flavour is, there will desire be also.

Insufficient ingestion, absorption, or assimilation of proteins, or of proteins of the right kind, will tend to degradation of vital processes—a degradation manifested in stunting of growth, poor physique, lack of energy, resource, and initiative, digestive disturbances, and impaired action of glandular organs. To these may be added a lowered resistance to infection. Severe degrees of protein starvation, associated as they often are with want of food in general, may give rise to a condition

known as 'malnutritional oedema', 'war oedema', or 'famine oedema', in which the body, in part or in whole, becomes water-logged.

#### PROTECTIVE FOODS

It will have been noted how frequently the names of certain foodstuffs—such as milk, green and root vegetables, and whole cereal grains—recur in the lists I have given to those rich in vitamins, minerals, and proteins. These are the protective foods, so called because they are rich in those substances which protect the body or its constituent parts against disturbance of structure or of function, or of both—that is to say, against disease. It is these foodstuffs which must be brought within the financial reach of everyone in the country and used by everyone if health is to be maintained. The last war resulted in a great increase in knowledge of the relation of food to nutrition and health; the present war already demonstrates the need to apply it—a need which day by day becomes more urgent.

Many factors interfere with the adequate supply or utilization of essential nutrients. Poverty, ignorance, indifference, habit, soil deficiencies, sophistication of natural foodstuffs, bad cooking, fads and fancies—all may interfere with adequate supply. Gastro-intestinal disorder and other bodily conditions may interfere with adequate utilization. In the presence of gastro-intestinal disorder defective utilization becomes dominant. Inadequate supply may itself impair appetite and set up gastro-intestinal disorder, thus interfering with utilization and establishing a vicious circle. It is rare that we have to deal only with a single deficiency in the diet. It is more usual for deficiencies to be multiple, and more usual still for multiple deficiencies—whether of vitamins or minerals or both—to be associated with the excessive richness of the food in carbohydrates. Thus the manifestations of ill-health resulting from the faulty food are compounded of the several effects of varying degrees of vitamin and mineral deficiency on the one hand and of carbohydrate excess on the other. Nor is this all, for infection by microbic agents usually contributes to the general morbidity.

#### DIETETIC MALNUTRITION

Malnutrition produced by faulty food should be spoken of as 'dietetic malnutrition'. It is widespread in its distribution, and is preventable only by readjusting our ways of life—social, agricultural, and economic—so as to ensure for everyone a diet that will satisfy physiological needs. Owing to the substitution of artificial feeding for mother's milk infants become subject to gastro-intestinal and pulmonary disease, to which they frequently succumb. Fretfulness, restlessness, anaemia, imperfect calcification and growth are other symptoms of malnutrition in infants. In early childhood malformation of the bones, dental defects, and abnormalities of the pharynx are alarmingly common and are consequences of dietetic malnutrition and faulty nurture. Consequent on malnutrition, children of this age have a lowered resistance to infections, are poorly grown, under height and weight, and have nervous systems that lack stability.

During adolescence the lowered resistance of the malnourished fosters the occurrence of tuberculosis. Girls reach womanhood with deformed pelvis which make child-bearing difficult or precarious, while faulty nutrition during pregnancy is a serious menace to both mother and child. Middle life and advancing age is for many a period of physiological decay and long suffering caused by chronic illness.

So from infancy and childhood through adolescence to adult life, dietetic malnutrition, aided often by infection, leaves its trail of morbidity, and this although the food faults may not be extreme. So long as they are sufficient in degree to impair the function of nutrition they will, sooner or later, directly or indirectly, give rise to disease. The constant drip will wear away the stone; the constant imperfection of nutrition, though this be relatively slight, will wear away the body. This dietetically caused imperfection of the

function of nutrition and the ailments resulting from it can be prevented by the use of a diet into which milk and its products, fresh green vegetables, root vegetables, particularly potatoes, and whole cereal grains, either in the form of oatmeal or of wholemeal bread, or both, largely enter. Thus we arrive, though by another path, at the same conclusion to which Professor J. C. Drummond's historical survey had led us.

## Clinical Studies in Non-Dysenteric Intestinal Amœbiasis

By JAMES J. SAPERO

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XIX, November 1939, p. 497)

DIVERSE opinions are held regarding the pathogenic rôle of *Entamoeba histolytica* in cases of intestinal amœbiasis which present neither a present nor past history of dysentery. Certain clinicians tend to attach clinical significance only to the dysenteric manifestations of the organism; others attribute to *E. histolytica* a wide range of protean symptomatology. Although the viewpoints of the majority are at neither of these two extremes, there is a considerable lack of agreement as regards both the nature and the frequency of symptoms in amœbic infections and their clinical importance when dysentery is absent.

Dobell in his monograph states that probably less than 10 per cent of persons who become infected with *E. histolytica* ever suffer to any appreciable extent from their parasitism. Faust believes that 90 to 95 per cent of persons harbouring the organism are apparently symptomless carriers. More recently, Wenrich, Stabler, and Arneth noted little evidence of pathogenicity in carriers found in an examination of college students, and observed that a control group seemed to have as many or more signs of ill health than those in their series who were carriers of *E. histolytica*.

Findings contrary to these have been reported by other workers. Craig, who had had wide experience, states that about 65 per cent of carriers have had symptoms referable to their infection, and that these symptoms disappeared after the eradication of the parasite. Philpitschenko reports that one-half of 400 apparently healthy carriers found in a survey of Leningrad food handlers had various intestinal disorders. Johnstone and his co-workers found that 52 out of 92 infections among a prison group were associated with notable gastro-intestinal upsets.

In addition to the discrepancies in the frequency with which symptomatology is associated with *E. histolytica* infections, it is to be noted that agreement is also lacking regarding the nature of the symptoms. Certain observers have incriminated the organism as the causative agent of symptoms far remote from the gastro-intestinal tract. Boyers, in an analysis of 1,961 complaints presented by persons found to be infected, believes his results show symptomatology referable to many other systems of the body. Craig, although mainly emphasizing the gastro-intestinal manifestations, notes that frequently nervous and circulatory disorders are attributed to *E. histolytica*. Arthritis, iritis, Hodgkin's disease and other conditions have been suspected of being caused by the organism, but no convincing ætiological relationship has been demonstrated in such cases and those claims have not at present gained any acceptance.

Many features lend particular importance to the problem of non-dysenteric amœbic infections. Primarily to be considered is the concept that *E. histolytica* is an obligate tissue parasite and that in every individual harbouring the organism there is a process of invasion and repair accompanied by more or less injury, the amount of disease, in all probability, being dependent on host resistance. As reliable estimates place the incidence of the organism to be about 10 per cent in the United States, it becomes important to reach some agreement on what proportion of the cases of amœbiasis shows evidence of injury.

### Analysis of signs and symptoms

**Physical signs.**—One of the most striking findings was the presence of abdominal tenderness. No less than 29 out of 46 gave this sign. The most prominent localization was at McBurney's point. In several instances this sign was so marked that had the individual complained concurrently of the symptoms encountered in appendicitis, operation would have appeared advisable. Circulatory abnormalities were not observed.

**Nature of symptoms.**—An analysis was made of 47 cases in which there was no ætiological factor other than the parasitic infection which would adequately explain the syndrome. To these were added seven cases in the control group who, although admitted for treatment for some unrelated condition, were found to be suffering concurrently with symptoms referable to their *E. histolytica* infections.

*Subjective complaints and objective signs in 54 hospital cases harbouring E. histolytica in which no other ætiological factor would adequately explain the syndrome*

Past history:—			
Dysentery	..	..	0
Appendicitis	..	..	24
Present history:—			
Nausea	..	..	20
Vomiting	..	..	6
Distention or flatulence	..	..	18
Heartburn	..	..	12
Abdominal pain	..	..	50
Epigastric	..	..	13
Umbilical	..	..	9
Right lower quadrant	..	..	14
Left lower quadrant	..	..	5
Generalized	..	..	9
Bowel movements, normal	..	..	28
Bowel movements, abnormal	..	..	26
Diarrhœa	..	..	9
Constipation	..	..	12
Diarrhœa and constipation	..	..	5
Headaches	..	..	16
Fatigability	..	..	14
Nervousness	..	..	10
Loss of weight	..	..	7
Physical signs:—			
Tenderness, abdominal	..	..	37
Epigastric	..	..	7
Cæcum	..	..	18
Ascending colon	..	..	7
Transverse colon	..	..	8
Descending colon or sigmoid	..	..	10

Almost one-half had at some recent time come under observation for appendicitis. Occasionally, upper gastro-intestinal complaints occurred to the exclusion of all other complaints. Pain was the most frequent symptom. The bowel movements were normal in over one-half of the cases. Constipation was a more frequent complaint than diarrhœa, this latter symptom occurring in but a small proportion of the cases. Nervous and circulatory disorders occurred but almost always in association with and subordinate to the gastro-intestinal complaints. Tenderness in various regions of the colon was elicited in 37 of the 54 cases and again the sign was commonly localized over the cæcum.

*Tentative admission diagnoses on 47 cases in which later clinical study revealed no adequate cause to explain the syndrome other than the presence of E. histolytica*

	Number of cases
Appendicitis, subacute or chronic	18
Peptic ulcer or chronic gastritis	10
Enteritis, chronic	7
Gall-bladder disease	4
Gastro-enteritis, acute	3
Appendicitis, acute	3
Renal colic	2
<b>TOTAL</b>	<b>47</b>



The tentative admission diagnoses made in 47 cases demonstrate the wide variation of conditions simulated by amoebic infections. The large number of cases thought to be appendicitis is consistent with other observations recorded in this series. Of those cases which came to operation, only those were included in which the pathological report of the appendix revealed no evidence of disease. It is to be noted that the larger number of cases were considered subacute or chronic manifestations of appendicitis, most of which were discharged without operation.

The most frequent was pain, being presented by 34 out of 47 cases. In three of the cases the complaint was mainly of weakness and in one the chief symptom noted by the patient was headache.

*Chief complaint in 47 cases harbouring E. histolytica in which there was no adequate cause to explain the syndrome other than the presence of the organism*

Pain .. .. .	34
Epigastric .. .. .	11
Umbilical .. .. .	5
Right lower quadrant .. .. .	8
Generalized .. .. .	8
Lumbar .. .. .	2
Nausea .. .. .	1
Constipation .. .. .	4
Diarrhoea .. .. .	3
Alternating constipation and diarrhoea .. .. .	1
Headache .. .. .	1
Weakness .. .. .	3

*Results of treatment.*—Carbarsone in 0.25 gramme capsules administered twice daily for a period of 10 days was given as a routine. The follow-up examinations were made between six and twelve months after treatment. Approximately three-fourths obtained relief following carbarsone administration. Although but few cases are included in which no treatment was given, it is of interest that the results were exactly opposite, the majority stating either that their symptoms had persisted or had become aggravated.

#### COMMENT

Judging from the rarity with which diagnoses of non-dysenteric phases of amoebiasis are made in medical practice, and considering the prevalence of *E. histolytica*, one would come to the conclusion that clinical manifestations of the organism without dysentery are rarely of such severity as to require medical assistance. In the present investigation, however, quite the contrary proved to be so. Even in what may be presumed to be a highly resistant group, some of the infected individuals presented complaints which could not be regarded as unimportant. In the hospital study an impressive number of cases proved to be of amoebic origin and, had not the presence of the parasite been demonstrated, the final diagnoses in these cases would have fallen in that large and unsatisfactory group in which neither the true cause nor the nature of the disorder is known.

The most striking feature of the cases studied in the investigation was the dissimilarity of their clinical manifestations as compared to the symptomatology encountered in amoebic dysentery. Whereas the presence of dysentery, or blood and mucus in the stools immediately brings to mind the possibility of an amoebic process, the same organism is capable of producing disorders which give but scant clues to the nature of the disease. This observation becomes of greater importance in view of the fact that the largest proportion of amoebic infections are of this latter type. This was demonstrated in a recent naval survey in which only 4.6 cases of dysentery were found for each 1,000 individuals harbouring *E. histolytica*. Thus, despite the less serious nature of the non-dysenteric cases of intestinal amoebiasis as compared with those presenting dysentery, the difficulties in their diagnosis

and their prevalence constitute a problem of some importance in clinical medicine.

It appears that a large number of apparently obscure gastro-intestinal cases which seek relief in hospitals and clinics are actually cases of amoebiasis and that frequently these cases are not being diagnosed. The lack of recognition of the non-dysenteric syndromes is due to the fact that a positive diagnosis is dependent on the demonstration of the organism in the stool examination. It is known that rarely should the organism be reported in any less than 5 per cent of routine stool examinations, yet too often hospital laboratory reports fail to reveal any such incidence of infection. Where this is so, the infections cannot be diagnosed and this situation has led to a false impression regarding the clinical importance of non-dysenteric manifestations of *E. histolytica*.

Certain clinical aspects of these cases are characteristic enough to bring to mind the possibility of an amoebic infection and lead to an intensive search for the parasite by stool examination. From the clinician's standpoint, a clear understanding that blood and mucus need not be associated with amoebic infections is of fundamental importance. Usually the non-dysenteric case is first suspected of being some well-defined and common gastro-intestinal entity, but a study shows so much to be atypical that the anticipated diagnosis cannot be reached. It is this very atypicalness which should suggest amoebiasis, and with abdominal pain as a prominent complaint, and when the symptoms are characterized by chronicity and recurrency, these features all become especially suggestive of amoebiasis.

Of special interest in the present investigation was the common occurrence of a syndrome simulating subacute or chronic appendicitis. Appendicitis was particularly apt to come under consideration in the disorders encountered in these groups, but the frequency with which the various attending physicians were led to consider the possibility of disease of the appendix was a striking feature of the investigation and one which indicated the organism to have an important rôle in such syndromes. The possibility of a large proportion of the non-dysenteric cases suffering from an amoebic typhlitis suggests itself. Many of the cases harbouring the organism were subjected to operation. In none of the infections were ill-effects noted as a result of operation, and in a few, serious results undoubtedly would have followed had operation been withheld. The significant fact was that in many cases the signs were too mild to indicate surgery, while in others there was a return of like symptoms after operation, these facts suggesting the advisability of anti-amoebic therapy in connection with other indicated treatment in these cases.

#### SUMMARY

In the present clinical investigation only cases of intestinal amoebiasis in which there was neither a present nor a past history of dysentery were studied. The cases comprised both symptomless carriers of *E. histolytica* and infected individuals with complaints of varying severity. Control observations were made whenever feasible. Only those symptoms and signs were ascribed to *E. histolytica* after other possible causes had been ruled out. In all, 216 cases of non-dysenteric amoebiasis were studied, of which 100 were found to have symptoms.

1. A study of the occurrence of symptomatology in a selected group of 106 apparently healthy men harbouring *E. histolytica* showed 46 or 43.4 per cent to have symptoms. A control group of 108 cases negative for intestinal protozoa revealed but 8 or 7.4 per cent to have complaints. Of the 106 cases of amoebiasis only 13.2 per cent of the complaints were of any appreciable severity.

2. Of 236 individuals harbouring various intestinal protozoal species, but not *E. histolytica*, the percentage with symptoms was similar to that found in the non-parasitized group, with the exception of *Dientamoeba fragilis* in which 27.3 per cent of 44 cases presented

symptoms. Similarly, some of the flagellates presented higher percentages than the control. An explanation of this apparent pathogenicity was offered.

3. A study of the blood findings in 61 cases of apparently healthy carriers of *E. histolytica* showed no significant differences from the results obtained in a control group of an equal number of individuals not harbouring the parasite.

4. Despite the apparent trivial nature of the complaints presented by most of the cases in an ambulatory group, it was found by a study of various hospitalized groups that a considerable number of non-dysenteric amoebic infections are severe enough to require hospitalization. In 47 such cases the disease picture was so obscure that only the finding of the parasite in the stool led to the proper diagnosis, and

in these, specific anti-amoebic treatment gave good results where other methods had failed.

5. A study of the nature of complaints revealed these to be primarily referable to the gastro-intestinal tract, yet without blood and mucus in the stools and usually without bowel abnormalities which might suggest an amoebic process. Complaints referable to both upper and lower gastro-intestinal tracts appeared with equal frequency. Complaints referable to other systems were seldom encountered. Chronicity, recurrence and mildness of the symptoms were characteristic features.

6. A symptom-complex simulating subacute or chronic appendicitis was the most commonly observed syndrome in this series of non-dysenteric cases of amoebiasis.

## Reviews

**THE BRITISH ENCYCLOPÆDIA OF MEDICAL PRACTICE INCLUDING MEDICINE, SURGERY, OBSTETRICS, GYNÆCOLOGY AND OTHER SPECIAL SUBJECTS. SURVEYS AND ABSTRACTS. 1939.** Under the General Editorship of Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., D.Sc., D.C.L., LL.D. Pp. xiii plus 605 plus 50. Illustrated

and

**CUMULATIVE SUPPLEMENT. 1939. Pp. 170.** Published by Butterworth and Company (Publishers), Limited, London. Obtainable from Messrs. Butterworth and Company (India), Limited, Calcutta. Price of these two volumes inclusively is Rs. 18-8

THE publishers of the *British Encyclopædia of Medical Practice* have always expressed their intention of keeping this ambitious publication alive by issuing supplementary volumes year by year. That they have kept this promise in the trying circumstances of the year 1940 is very much to their credit. Two supplementary volumes have been issued.

*Surveys and Abstracts, 1939.* This volume consists of twenty-five critical surveys with such general headings as General Medicine, Diseases of the Blood-forming Organs, Pharmacological Aspects of the Endocrines, and Tropical Medicine, and some more specific ones, such as Q-Fever, Contact Lenses, and Acute Rheumatism. The writers are all well-recognized authorities on their own subjects. There follows a short section on drugs; some Modern Drugs by Dr. P. Hamil and the Pharmacology of the Sulphonamide Drugs by the publishing editor, Dr. Clark. The rest of the volume consists of abstracts from the literature arranged under headings which more or less correspond to the headings in the twelve volumes of the encyclopædia.

The majority of the critical surveys are excellent, but in a few instances the writer didn't seem to know quite what he was really setting out to do and the result was a short résumé of a very wide subject, which didn't hold well together or give the reader any information that he could not have obtained from the original article in the earlier volumes.

The abstracts are taken from a wide range of medical journals, including British and British Empire journals, American, and European other than British. These for the most part are well chosen and well arranged, but there are a number of isolated extracts which, divorced from their context, appear, to the reviewer, to be more or less meaningless, e.g., Methylene Blue Reaction, and Formol-gel and Takata-Ara Reactions.

*The Cumulative Supplement.* If the above volume is a little uncertain in its purpose, there is no uncertainty about the purpose and value of this cumulative supplement. The headings followed are those

of the original encyclopædia and in each the volume and key numbers of the original articles are given in the margin. Whenever a subject has been adequately dealt with in *Surveys and Abstracts* this fact is noted, but in other instances a short note is given which is strictly supplementary to the original article and which brings the subject up to date. Not only are these short articles clearer in their purpose, but they are in most instances much more balanced and relevant contributions to their various subjects than those provided in the other volume. We sincerely hope that the supplement will meet with the success that it deserves and that the publishers will be able to keep to their original purpose of issuing this cumulative volume each year.

**HÆMORRHOIDS AND THEIR TREATMENT: THE VARICOSE SYNDROME OF THE RECTUM.**—By Kasper Blond, M.D. (Vienna). Translated by E. Stanley Lee, M.S., F.R.C.S. 1940. John Wright and Sons Ltd., Bristol. Simpkin Marshall Ltd., London. Pp. viii plus 140, with 49 illustrations, many in colour. Price, 15s.

THIS is a monograph of outstanding merit and one which will meet with a cordial welcome. For the English translation much credit is due to Mr. Stanley Lee. The injection treatment of hæmorrhoids will cause no surprise or comment anywhere. But the author's conception of ætiology and treatment of fistula and pruritis will be new to many readers. The concept of the portal system, and its rôle in the formation of hæmorrhoids, will be not merely new but startling to many of us. The author has described under the heading of 'Varicose Syndrome of the Rectum' a number of conditions such as pruritis, anal fissure and fistula, etc., which are generally regarded as separate entities. The author is of opinion that all pathological conditions which impede the portal venous return may thus play a part in the development of hæmorrhoids and allied lesions. There is considerable evidence in support of the author's concept.

The printing, get-up and illustrations are excellent. We strongly commend this book to the notice of the general practitioner.

P. N. R.

**DISEASES OF THE URETHRA AND PENIS.**—By E. D'Arcy McCrea, M.D., M.Ch. (Dub.), F.R.C.S.I., F.R.C.S. (Eng.). 1940. John Wright and Sons Ltd., Bristol. Simpkin Marshall Ltd., London. Pp. viii plus 306, with 181 illustrations, many in colour. Price, 21s.

THE author explains in the preface that this volume represents an attempt to give in some detail an account of present-day knowledge of diseases of the urethra and penis and to provide an easy reference to the literature on the subject.



There are altogether sixteen chapters in this book, with clear descriptions of regional anatomy, malformation, injuries, diseases and new growths of the penis and urethra. This book may rightly be regarded as an important monograph and will be much appreciated by the general practitioner. The printing, get-up and illustrations are excellent.

P. N. R.

**A HANDBOOK OF RADIOGRAPHY.**—By J. A. Ross, M.A. (Camb.), M.R.C.S. (Eng.), L.R.C.P. (Lond.), D.M.R.E. (L'pool). 1940. H. K. Lewis and Company, Limited, London. Pp. viii plus 126, with 67 illustrations. Price, 7s. 6d.

THIS small book was read with great interest by the reviewer; it gives in clear and simple language all that should be known about radiography accompanied by simple line illustrations.

The descriptions of the technique are adequate, and the printing, get-up and illustrations are excellent.

The book will prove extremely valuable to both the radiologist and radiographer.

E. H. W. F.

**A MIRROR FOR SURGEONS: SELECTED READINGS IN SURGERY.**—By Sir D'Arcy Power, K.B.E., F.R.C.S. 1939. Little, Brown and Company, Boston (34, Beacon Street, Boston, Massachusetts). Pp. xii plus 230. Price, \$2.00

THIS is a contribution to the history of medicine of a kind we are beginning to associate with the name of Sir D'Arcy Power.

The book contains vignettes of twenty-two well-known surgeons ranging over the years 1307 to 1924. The first date being the birth of Master John Arderne, 'the first British surgeon', and the second the date of Sir William MacEwen's death.

Each section begins with a few lines indicating the upbringing and family life of the surgeon concerned, and this is followed by one or more quotations from the surgeon's own writings on his chief contributions to surgical practice.

The book makes an interesting and valuable contribution to the history of medicine, and reading it serves to pass a few hours pleasantly and profitably.

We notice it is published in the United States of America although the author is one of the leaders of British surgery. By publication overseas the book has lost nothing from the point of view of production for the binding, printing and kind of paper used are most appropriate for the contents of the book.

**SEX KNOWLEDGE FOR BOYS. VOLUME ONE AND SEX KNOWLEDGE FOR GIRLS. VOLUME TWO.**—By A. P. Pillay, O.B.E., M.B., B.S. Published by D. B. Taraporevala Sons and Company, Hornby Road, Fort, Bombay. Volume I:—Pp. vi plus 72, with 5 illustrations. Price, Re. 1-8. Volume II:—Pp. iv plus 66, with 5 illustrations. Price, Re. 1-8.

MANY parents look with disfavour and sometimes harshness on any signs of sex knowledge on the part of their children. It is now, however, being increasingly recognized that some form of sex education should be given to children, in view of the evil results of early inhibitions and repressions during the most impressionable period of puberty. Hence the presentation of the facts of sex to the young in a popular style will meet an important need.

These two volumes of 'facts of life' series provide simple and common sense information about sex for boys and girls. Starting with the reproduction of plants, birds and mammals the author finally tells as much about human sex life as a growing child should know. The physical and psychic problems of sex, masturbation, the hygiene of sex, etc., have been dealt with concisely in a practical manner with a summary following each section. Many of the facts and illustrations are common in both books. There is a glossary at the end of each.

R. C.

**A HANDBOOK OF MALARIA CONTROL.**—By R. Svensson, D.S.O., M.C., M.B., B.Ch. With a Foreword by Sir Malcolm Watson, LL.D., M.D., C.M., D.P.H., F.R.F.P.S. Published by the Shell Group of Oil Companies for The Ross Institute of Tropical Hygiene, Keppel Street, Gower Street, London, W.C.1. Pp. viii plus 73. Illustrated.

MUCH patient labour has been usefully expended in the compilation of this small handy treatise, which it is hoped will satisfy the need of a simple compact reference book on certain aspects of malaria control work for the use of planters, engineers, and other laymen who have to undertake antimalaria work in the tropics. Although the book is not primarily intended for medical men, nevertheless, they will also find it useful at times.

The book is divided into 11 chapters and 11 appendices. Such useful subjects as collection, preservation and dissection of mosquitoes, bionomics of carrier species, etc., have not been overlooked.

D. N. R.

**MEDICAL RESEARCH COUNCIL. SPECIAL REPORTS SERIES, NO. 238. 'THE STRUCTURE OF TEETH AS SHOWN BY X-RAY EXAMINATION'.**—By J. Thewlis. 1940. Published by His Majesty's Stationery Office, London. Pp. 82. Illustrated. Price, 2s. 6d.

'ONE of the main problems of dental research is that of caries, and it is becoming increasingly apparent that liability to this disease is related to defective structure of the teeth. The nature of the structural defects concerned is not precisely known, although certain manifestations of such defects are recognizable both by the naked eye and microscopically.

It is not unreasonable to assume that these defects may be related to the submicroscopic structure of a tooth, of which something has been learned by the use of the x-ray diffraction technique used by Mr. Thewlis. This method has been successfully applied for a long time in various technical branches of science, but has nevertheless been little used in biology. That it has definite biological applications, however, may be seen from the present report, in which the nature, size and arrangement of the crystalline particles in teeth are shown to have been ascertained by its use.

Optical methods have also been employed in the investigation, but apart from x-ray diffraction chief use has been made of the radiographic method, perhaps more familiar than the others to the majority of readers. The radiographic method, however, has been adapted to the special needs of the work and has been so developed as to make possible the quantitative determination of the degree of calcification in different regions of the enamel and dentine in a given tooth, or indeed in any calcified tissue. It has been usual to control estimates of the degree of calcification in teeth by histological methods, the accuracy of the results of which cannot be guaranteed. This highly specialized and applied study of the problem by Mr. Thewlis has yielded valuable and unquestionable information more exact than histological examination could possibly provide.'

**MEDICAL RESEARCH COUNCIL. SPECIAL REPORTS SERIES, NO. 241. 'DENTAL DISEASE IN THE ISLAND OF LEWIS'.**—By J. D. King. 1940. Published by His Majesty's Stationery Office, London. Pp. 63. Price, 1s.

THE superiority of the teeth of the average country child in Lewis, as regards both sound formation and freedom from decay, has been placed beyond dispute by the evidence here presented. From a general standpoint, chief interest naturally attaches to the reasons for this enviable quality. Here, however, the data are less adequate as a basis for firm conclusions: the possible factors are complex, and points relating to mode of life are difficult to ascertain with completeness and accuracy. Nevertheless, all the positive indications support the viewpoint that only differences in diet

can explain the facts, and no other differences of a relevant kind have been found. These indications include the consumption of a relatively high proportion of fat-soluble vitamins and mineral salts, the nutritional factors which have been experimentally proved to be essential for the proper development and calcification of the teeth. In other respects, such as the amount of carbohydrate and the physical consistency of the food, the diets of the rural and urban children in Lewis did not seem to be notably different.

The more favourable diet of the country children is due to the inclusion of a greater proportion of natural produce, and a lesser dependence on bought foodstuffs poor in protective factors. This in turn is related to distance from the shopping centre and to difficulties of transport. It is therefore conceivable that, under the impact of changing conditions, the local advantage may already be waning. The evidence stands, however, to show once again that dental disease is to an important extent preventable by correct nutrition, and that means of diminishing this evil are therefore within the scope of public administrative action.

The value of such a study and the application of its findings to conditions in India are obvious.

**MEDICAL RESEARCH COUNCIL. SPECIAL REPORTS SERIES, NO. 242. 'STUDIES IN NUTRITION: AN INQUIRY INTO THE DIET OF FAMILIES IN THE HIGHLANDS AND ISLANDS OF SCOTLAND'.**—By E. P. Cathcart, A. M. T. Murray and J. B. Beveridge. 1940. Published by His Majesty's Stationery Office, London. Pp. 37. Illustrated. Price, 9d.

'Among the basic data for research on human nutrition, and for application of scientific knowledge to its practical problems, it is clearly necessary to have definite information as to the actual diet of the people: this can be obtained only by careful and laborious studies of samples of the population. Professor E. P. Cathcart of the University of Glasgow, with assistance by Mrs. A. M. T. Murray and others, has made a number of surveys of this kind in different parts of Great Britain.

The present report deals with a study made in the Highlands and Islands of Scotland.

The method used in the survey was to select a number of families and ascertain the food intake of each during a period of one week. The original studies in the Highlands were made in summer, but duplicate studies of some of the same families were made in winter; this was done partly to reveal any seasonal variations, and partly as a check on the reliability of a single week's observations as an index of the diet as a whole. As on a previous occasion, the investigators found from the evidence obtained in this way that their method was sound, although there were naturally some differences between foods consumed in summer and winter respectively.

As already indicated, the diet can be considered from the standpoint of fundamental constitution (protein, fat, carbohydrate, minerals and vitamins) and energy value (expressed in calories), or it may be considered with regard to the actual food commodities which make up the diet. In this report the results of both methods of analysis are given.

**THE DIAGNOSIS AND TREATMENT OF DIABETES.**—By W. Willson Ingram, M.C., M.D., F.R.A.C.P. Third Edition. 1940. Angus and Robertson Limited, Sydney. Pp. ix plus 150. Price, 6s. 6d.

This book has been designed primarily for the use of general practitioners and gives a simple outline of those facts regarding diabetes, a knowledge of which is essential for the successful treatment of the disease.

The book has been written in a very simple and clear style and should prove to be very useful to both the practitioner and the medical student. The text is quite up to date.

A new chapter has been added on the new insulin compound—protamine zinc insulin—and a new outline

of diet has been added for those patients who are on this modified insulin.

A short chapter has also been added on the management and treatment of diabetic children.

The book contains valuable information and should prove useful to those for whom it is intended.

J. P. B.

**THE DIABETIC A. B. C. A PRACTICAL BOOK FOR PATIENTS AND NURSES.**—By R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.). Seventh Edition. 1940. H. K. Lewis and Company, Limited, London. Pp. vii plus 64. Price, 3s. 6d.

LITTLE comment is necessary on the seventh edition of Dr. Lawrence's practical book for patients and nurses, the predecessor of which we had the pleasure of reviewing a little over a year ago. No radical changes appear to have been made in the present edition except that a few new diabetic recipes have been added.

We hope the book will continue to be as useful and popular as its predecessor.

J. P. B.

**PRACTICAL HANDBOOK OF THE PATHOLOGY OF THE SKIN: AN INTRODUCTION TO THE HISTOLOGY, PATHOLOGY, BACTERIOLOGY AND MYCOLOGY OF THE SKIN WITH SPECIAL REFERENCE TO TECHNIQUE.**—By J. M. H. Macleod, M.A., M.D., F.R.C.P. (Lond.), and I. Muende, M.B., B.S., B.Sc. (Lond.). Second Edition. 1940. H. K. Lewis and Company, Limited, London. Pp. xix plus 415, with 27 coloured and 125 black-and-white illustrations. Price, 42s.

THIS book is accurately described in its title and sub-title (given above) for that is exactly what it is.

The unusually long period of 37 years has passed since the appearance of the first edition under the authorship of Dr. Macleod alone. That the same author was sufficiently experienced to produce a valuable book so long ago and that he has been actively engaged upon the study of dermatology ever since is sufficient evidence that the present edition must be a valuable book.

Considering the many advances that have been made in pathology and biochemistry since 1903 the character of the book is changed to a remarkable small degree and it contains only a few more pages than its predecessor despite the fact that the number of illustrations has been considerably increased. At the same time there is a definite addition to the amount of the text, which is masked by the fact that the pages of the new edition are about 20 per cent larger than those of the old one.

If we may select a section for special comment without in any way indicating that the rest of the book is not also excellent, we feel that the portion dealing with mycology is particularly useful, because it gives a short and clear summary of the essentials of what is a most confusing and unwieldy subject for a beginner to acquire a working knowledge of, from the books that are usually available. This makes the book of special value to tropical dermatologists, such a large proportion of whose cases are caused primarily by a fungus of some kind, and it is sure of a ready sale in the tropics.

P. A. M.

**THE CONTENT OF CELLS AND PROTEINS IN THE NORMAL CEREBRO-SPINAL FLUID: THE DIAGNOSTIC IMPORTANCE OF DEMONSTRATING SMALL PATHOLOGICAL CHANGES IN THE CELLS AND PROTEINS—THE TECHNIQUE OF THE INVESTIGATION.**—By A. V. Neel, M.D. Oxford University Press, London, Humphrey Milford. Pp. 141. Price, 7s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

THIS is the report of studies carried out in Copenhagen by the author. It is remarkable how poor and inaccurate are our normal data for many of the examinations that form part of our daily practice.

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## BENGAL CHEMICAL AND PHARMACEUTICAL WORKS, LD.

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Studies of this kind are very important and should be fully reported wherever possible. This book should find a place in the libraries of all medical teaching institutions.

**A SYNOPSIS OF THE BRITISH PHARMACOPŒIA, 1932, AND OF THE POISON LAWS OF GREAT BRITAIN, NORTHERN IRELAND AND THE IRISH FREE STATE, INCLUDING THE 1936 POISONS LIST AND RULES.**—By H. Wippell Gadd. Thirteenth Edition. 1936. Baillière, Tindall and Cox, London. Pp. 200. Price, 3s. 6d.

THIS well-known *Synopsis* has been brought up to date by two synopses of the 1936 and 1940 addenda to the *British Pharmacopœia* 1932.

**THE PRACTITIONER'S POCKET-BOOK.**—By D. S. Davies, D.M. (Oxon.), F.R.C.S. (Edn.). 1939. John Bale Medical Publications Limited, London. Pp. 266. Price, 7s. 6d.

THIS is the sort of book a physician might keep in his car. It is a pocket-book size, but there is already a fair demand on the physician's pocket. The descriptions are incredibly concise, and frequently very

apposite. For example, there are six lines on the treatment of cholera; they include instructions in giving intravenous saline and the terse remark 'never give morphine', amongst other good advice. (We cannot however agree that the incubation period is 2 to 8 days.)

Other subjects simply will not compress and the result of the attempt is rather disastrous. However, on the whole, the balance is in favour of the book if it is kept out of the hands of the student.

**IRVING'S ANATOMY MNEMONICS.**—By Alastair G. Smith, L.R.C.P. & S. (Edn.). Fourth Edition. 1939. E. and S. Livingstone, Edinburgh. Pp. 133. Price, 1s. 6d. Postage, 1d.

'To the simple-minded, to the crammers for exams, and to those whose stumbling feet find the anatomical pathway difficult, this little book is offered in the hope rather than the belief that they may find some help from it.'

So writes the author, and many will agree that mnemonics are a great assistance to the examinee.

This book which has now reached its fourth edition, will form a useful Christmas card to send to a medical student, as it is very cheap and will easily go into an ordinary envelope.

## Abstracts from Reports

### PUBLIC HEALTH COMMISSIONER'S PRELIMINARY REPORT FOR 1939

PUBLICATION of a preliminary report has been found advisable owing to unavoidable delay in preparing the full report, which contains a great deal of statistical and other material relating to the wide variety of health activities of the whole sub-continent of India.

In 1938, as the result of a widespread dissemination of infection following the Hardwar festival in April, all the provinces in Northern India and the Central Provinces suffered severely from cholera. The extent to which the incidence of cholera decreased may be judged from the figures for cholera deaths in the Punjab and Sind, in which provinces there were respectively 19 and 3 deaths in 1939 as against 5,760 and 343 in 1938. In other provinces, too, cholera prevailed in a relatively milder form.

It is reported that the incidence of plague also decreased in 1939 and that, in regard to smallpox, although the majority of the provinces reported epidemic prevalence of the disease, Bengal and Sind experienced only mild outbreaks.

In the field of public health administration, the most important event was the second meeting of the Central Advisory Board of Health in January 1939. This board, which consists of representatives of the Central and Provincial Governments and of certain Indian States, was inaugurated in June 1937 for the purpose of providing a forum for the discussion and formulation of public health policy. Within the short period of its existence it has already given proof of its usefulness.

The problems associated with the health of the mother and child are of supreme importance to every country and, in India, the high rates of child and maternal mortality place this branch of health work in the forefront of the national health programme. A special committee appointed by the board reviewed the whole question and submitted a report, which has been approved by the board and which should provide for many years a sound basis for the orderly development of maternity and child-welfare work in this country.

Another important question is that of co-ordinating the activities of the civil, military and railway health authorities in matters of common concern, in order to avoid unnecessary overlapping of effort. For this purpose the board suggested the formation of local committees representing all three interests for the

study of common health problems and for the formulation of suitable methods of solving these problems. Encouraging reports have been received regarding the development of such co-operation in many places.

The important part that festivals and large gatherings of pilgrims play in the spread of cholera is a subject of great concern to the health authorities. While an improvement of the sanitation of the villages and towns through which the pilgrims pass is the most effective means of prevention, its realization must be slow, in view of the cost involved.

In the circumstances, the most practical method of minimizing the spread of cholera appears to be the provision of mass protection through anti-cholera inoculation. The possibilities of introducing a system of compulsory inoculation among pilgrims was investigated in 1939 by a special committee and their report will shortly be presented to the board for its consideration.

Control of the purity of food supplies is an important function of health administrations, and one of the means of achieving this end is by the enforcement of the Food Adulteration Act. A committee was appointed by the board to report on the question of food adulteration in India and this committee held two meetings in 1939.

The problem has three aspects: (a) standards of purity for different articles of food and the standardization of the technique employed in food analysis; (b) food legislation and (c) administration.

In regard to the first the present position in India is very unsatisfactory. For the same article of food different provinces have different standards. This anomaly impedes the free flow of inter-provincial trade and causes considerable inconvenience to traders. The question of food standards has, therefore, been studied by the committee and its recommendations, which are calculated to relieve the existing complicated situation, will shortly be submitted to the board for its consideration.

The modernization of food legislation in India and the application of the provisions of such legislation by suitable administrative action are equally important aspects of the food adulteration problem.

Mention may also be made of other directions in which it has been sought to secure uniformity of policy between the different Governments in the improvement of health conditions. Common lines of policy have been recommended by the board regarding the expansion



of health services, co-ordination of effort between the medical and public health departments and the teaching of hygiene in medical schools and colleges.

Such subjects as nutrition and quinine policy have also been discussed by the board.

This brief review of some of the important subjects discussed and the recommendation made by the board, indicates that the wish expressed by His Excellency the Viceroy at the inaugural meeting of the Board in June 1937 is being increasingly fulfilled, namely, that the Board, 'in its capacity as an advisory body in organic union with the Central Government, will be capable of bringing to a common denomination the varied opinions of Governments throughout the sub-continent in matters pertaining to Public Health'.

**Malaria.**—That malaria is undoubtedly the most important public health problem in India is shown by the fact that many millions of cases occur every year and that, of the annual total of over 6,000,000 deaths, about 20 to 25 per cent are attributable to this cause.

Except for areas 5,000 feet above sea level and a few widely separated regions—namely, a portion of the Brahmaputra Valley in Assam, Eastern Bengal and two strips of territory on the east coast of Madras Presidency—the remaining parts of India are subject to outbreaks of malaria of varying intensities. This wide distribution of the disease and the liability of large tracts to periodical epidemic outbreaks make malaria the most important health problem in India.

The malaria problem in India may be classified under three heads—urban, industrial and rural. In large cities, such as Bombay and Delhi, it has been shown that a considerable measure of success in the control of mosquito breeding and of the incidence of the disease can be achieved by properly directed measures. As regards industrial malaria, control measures are being successfully carried out on many tea and coffee estates and rubber plantations and in mines, sugar factories, cotton mills and other industrial concerns in different parts of India, mainly through the activities of the Indian Branch of the Ross Institute.

Malaria control is also being carried out on railway systems, the Bengal-Nagpur and Eastern Bengal Railways employing special officers for the purpose. Among the anti-malarial measures adopted by the railway authorities, an important method is that of spraying employees' quarters with insecticides in order to kill adult mosquitoes.

The problem of rural malaria is the most difficult of solution, because the village communities are widely scattered and are very poor. The general policy adopted by the provincial authorities is to try and provide an adequate supply of quinine and of cinchona febrifuge, to popularize the use of these drugs as far as possible by means of propaganda and teaching in the schools, and to provide for distribution by special staffs, travelling dispensaries and other agencies in localities visited by regional epidemics.

Experiments are being conducted over a period of five years and are designed to devise and test out methods of control under rural conditions, in order that they may subsequently be applied over more extended tracts of the country.

**Leprosy.**—A conservative estimate of the incidence of leprosy in India places the figure in the neighbourhood of 1,000,000 persons affected, although the number of infectious cases may be only a quarter of this figure. While leprosy in India is essentially a rural problem, the commingling of the rural and urban populations that increased facilities for transport has rendered possible, has tended in recent years to produce a rise in the incidence of leprosy in towns.

The prevalence of the disease is highest along the eastern coast of the peninsula and in the western parts of Bengal. From this area the disease gradually diminishes in incidence to the north and west, until a fairly wide area of comparative freedom from leprosy is reached, comprising the northern half of Bombay Presidency, Gujerat, Rajputana, the western portion of the United Provinces, the Punjab, the North-West Frontier Province, Sind and Baluchistan.

Antileprosy work in India is shared by official and voluntary organizations. The principal voluntary organizations are the Indian Council of the British Empire Leprosy Relief Association with its provincial branches, and the Mission to Lepers. There is considerable co-ordination of effort between the provincial health authorities and the provincial branches of the British Empire Leprosy Relief Association. Antileprosy work has included surveys to determine the extent of the incidence of leprosy and of the types of cases present in particular localities, the provision of treatment centres, training of medical officers in the diagnosis and treatment of the disease, and propaganda. Laboratory and field research into various problems has also formed an important part of the work.

**Tuberculosis.**—Although the organized campaign against tuberculosis in India received a great impetus in 1929 when it was decided to devote the King George Thanksgiving Fund of Rs. 9,50,000 to antituberculosis work, the necessity for a widening and intensification of the campaign against the disease was recognized by Her Excellency the Marchioness of Linlithgow soon after her arrival in India. As a result, Her Excellency made an appeal on behalf of the King-Emperor for funds to place the antituberculosis organization in this country on a sound and lasting basis.

The response was wide and generous and a sum of Rs. 79,00,000 was collected. In February 1939, Her Excellency's objective was achieved by the formation of the Tuberculosis Association of India which incorporated the King George Thanksgiving (Anti-Tuberculosis) Fund. Of the total amount collected 5 per cent was retained by the central organization, the remaining 95 per cent being returned to the provinces. Provincial and state branches of the association were established during the year.

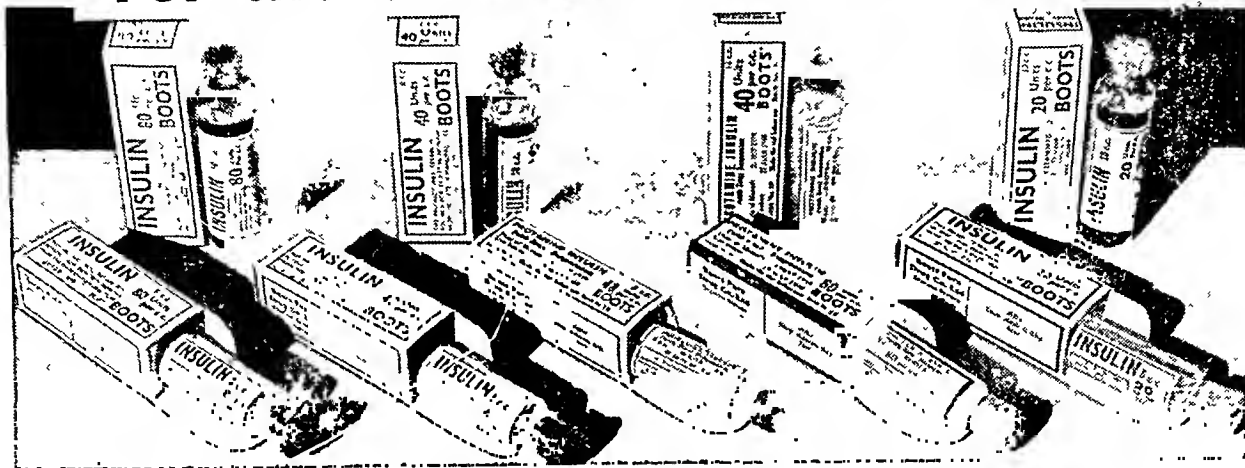
**Yellow fever.**—As regards yellow fever, the greatest source of danger is air traffic passing through the infected regions of Africa. Air traffic from Africa to India passes through the Anglo-Egyptian Sudan northwards to Europe and eastwards to India. The Sudan occupies, therefore, a central position and constitutes the main line of defence against the advance of yellow fever to Europe and Asia. The Government of India have taken additional precautions to prevent the entry of infection into this country. Under the Government rules, any person who has been in a yellow fever area is forbidden to enter British India until nine days have elapsed from the last date on which he was possibly exposed to infection, unless he has previously been inoculated against the disease or protected by a previous attack. Further, the entry into India of any aircraft which has alighted in or started from a yellow fever infected area is prohibited, unless the aircraft has been disinfected by the health authorities at Alexandria or Cairo and has a certificate to that effect.

**Dietary habits.**—A point of special importance to India is that, at a meeting of a special committee of the Technical Commission in August 1938, it was decided that collaboration should be extended to the Far Eastern countries in order to collect further information regarding the dietary habits, the incidence of diseases connected with dietary habits and the value of local foods. Dr. W. R. Aykroyd, Director of the Nutrition Research Laboratories, Coonoor, was present at the meeting and it has since been decided that the Coonoor Laboratory should act as a liaison centre between the Technical Commission and the various institutions engaged in nutrition work in Eastern countries.

**Epidemic dropsy.**—Epidemic dropsy is a disease which is widely prevalent in north-eastern India, for instance, in Assam, Bengal, Bihar, Orissa and the eastern parts of the United Provinces. The cause of the disease was for long a mystery in spite of considerable research done on the subject. Recently, however, it has been shown through epidemiological studies and the results of human feeding experiments, that the accidental contamination of mustard seed with the seed of a weed, *Argemone mexicana*, which grows wild in the fields where the mustard plant is grown, seems to be associated with the production of this disease.



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(Continued from page xvii)

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**PRACTICAL POINTS IN EYE SURGERY AND DRESSING.** For Nurses, House Surgeons and General Practitioners. By Hugh E. Jones, M.R.C.S. (Eng.), L.R.C.P. (Lond.). Rs. 2-3. (1933.)

**PRINCIPLES IN THE TREATMENT OF INFLAMMATION.** By T. E. Hammond, F.R.C.S. Rs. 7-14. (1934.)

**PUBLIC HEALTH PRACTICE IN THE TROPICS.** By J. Balfour Kirk, M.B., Ch.B., D.P.H., D.T.M. & H., Director, Medical Health Department, Mauritius. With 80 Illustrations. Rs. 13-2. (1931.)

**RADIOLOGICAL TERMINOLOGY.** By C. E. Galtskell, M.R.C.S., L.R.C.P. (Lond.). Rs. 3-12. (1935.)

**REFRACTION OF THE EYE: Including Elementary Physiological Optics.** By Charles Goulden, O.B.E., M.A., M.D., M.C. (Cantab.), F.R.C.S. Introduction by Sir John Herbert Parsons, C.B.E., F.R.C.S., F.R.S. Second Edition. 181 Illustrations. Rs. 9-6. (1938.)

**SCHISTOSOMIASIS (Bilharziasis).** By Dr. Rameses Girges, Tanta, Egypt. With a Foreword by Professor Ernest Carroll Faust. Illustrated. Rs. 18-12. (1934.)

**SHORT PRACTICE OF MIDWIFERY FOR NURSES.** By Henry Jellett, B.A., M.D. (Dublin University), F.R.C.P.I. Eleventh Edition. With 7 Plates and 182 Illustrations in the Text, also a number of Appendices and a Glossary of Medical Terms. Rs. 7-14. (1940.)

**SIMPLE INSTRUCTIONS FOR DIABETIC PATIENTS.** With Prescription Sheet for the Use of Patients, Nurses, and Practitioners. By Dorothy C. Hare, M.D., M.R.C.P. Second Edition. As. 12. (1935.)

**STUDIES IN THE AETIOLOGY OF DENTAL CARIES.** By G. Graham Macphree, M.A., M.D., Ch.B., L.D.S. Rs. 5-10. (1935.)

**SURGERY OF THE HAND: Wounds, Infections and Closed Traumatism.** A Book for the Practitioner and the Surgeon. By Marc Iselin, M.D., Surgeon, The American Hospital, Paris. Translated by T. J. d'Offay, M.B., Ch.B. (Edin.), F.R.C.S. (Eng.), and Thomas B. Mouat, M.D., Ch.M. (Edin.), F.R.C.S. (Eng.). With 135 Illustrations including 8 Plates. Rs. 18-6. (1940.)

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**SURGICAL SUTURES AND LIGATURES.** By E. J. Holder, B.Pharm., Ph.C. Illustrated. Re. 1-5. (1939.)

**TEXTBOOK OF HISTOLOGY FOR MEDICAL STUDENTS.** By Evelyn E. Hewer, D.Sc. (Lond.). Illustrated. Rs. 11-4. (1937.)

**THE CANCER PROBLEM AND ITS SOLUTION.** By Hastings Gilford, F.R.C.S. Re. 1-2. (1934.)

**THE CONSTITUTION AND ITS REACTION IN HEALTH.** By T. E. Hammond, F.R.C.S. Rs. 5-10. (1934.)

**THE CULTURE OF THE ABDOMEN.** The Cure of Obesity and Constipation. By F. A. Hornibrook. Preface by Sir William Arbuthnot Lane, Bart., C.B., M.S. Twelfth Edition. Illustrated. Rs. 5-4. (1938.)

**THE DIABETIC LIFE: Its Control by Diet and Insulin.** A Concise Practical Manual for Practitioners and Patients. By R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.). Tenth Edition. With 18 Illustrations. Rs. 4. (1937.)

**THE EARLY DIAGNOSIS OF MALIGNANT DISEASE.** By Geoffrey Kevnes, M.A., M.D. (Cantab.), F.R.C.S. (Eng.). Re. 1-14. (1935.)

**THE ESSENTIALS OF MEDICAL TREATMENT.** By David Murray Lyon, M.D., D.Sc., F.R.C.P. (Edin.). Rs. 13-2. (1939.)

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**THE FOOT.** By Norman C. Lake, M.D., M.S., D.Sc. (Lond.), F.R.C.S. (Eng.). Illustrated. Rs. 9-6. (1935.)

**THE HEALTH OF THE NATION AND DEFICIENCY DISEASES.** By John Maberly, M.R.C.S. (Eng.), L.R.C.P. (Lond.). Rs. 3-12. (1938.)

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**THE SURGERY OF THE SYMPATHETIC NERVOUS SYSTEM.** By George E. Gask, C.M.G., D.S.O., F.R.C.S. (Eng.), and J. Paterson Ross, M.S. (Lond.), F.R.C.S. (Eng.). Second Edition. Illustrated. Rs. 12. (1937.)

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**VACCINE THERAPY.** In Acute and Chronic Respiratory Infections. By Henry T. Gillett, M.D. (Lond.). With a Foreword by W. H. Wynn, M.D., F.R.C.P. With 9 Charts. Rs. 3-12. (1933.)

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**Endemic fluorosis.**—On a report in April 1936 from the Health Officer of Nellore district in Madras Presidency, regarding the wide prevalence of a disease characterized by a definite train of symptoms such as stiffness and pain in the spinal region and in various joints, a detailed study of this condition was carried out by the health authorities of that province and it was shown to be one of chronic fluorine intoxication resulting from the continued use of water containing fluorides. The problem is twofold, namely, the prevalence of a comparatively wide geographical area of a dental condition, commonly known as 'mottled enamel', and the occurrence in a restricted area, of severe manifestations of chronic fluorine intoxication involving the spine, joints and ligaments to which the name of endemic fluorosis has been given.

**Nutrition research.**—There has been a growing interest in problems of nutrition among the public and an increasing desire to apply the knowledge to the practical question of improving the existing diets within the means of the people.

This emphasis on the immediate application of the available information for the benefit of the country has largely influenced the direction in which nutrition research has developed in India in recent years. The Nutrition Research Laboratories at Coonoor, maintained by the Indian Research Fund Association, have taken a prominent part in these investigations. Rice as the staple food of a large section of the population received considerable attention in 1939.

Work on other foodstuffs included the determination of the vitamin-A content of a large number of samples of fish oils. Shark liver oil has been found to be exceptionally potent and this substance has considerable possibilities as a cheap source of vitamin A.

The vitamin-C content of the *amla* or Indian gooseberry, a very rich source of this vitamin, has been extensively studied by chemical and biological methods, special attention being given to the effect of storage and various methods of preparation and conservation.

**Increasing interest in rural health.**—There are signs of a growing interest both among the authorities and the people, in problems of public health. A welcome feature of this awakening to the seriousness of the existing situation is an increased interest in the welfare of the rural population. The expansion of medical relief, the provision of safe water-supplies, experiments to evolve a cheap system of night-soil conservancy and the provision of skilled attendance at childbirth are some of the directions in which provincial health authorities are earnestly endeavouring to make progress.

The Provincial Governments have increasingly interested themselves in improved agricultural practice and animal husbandry, the consolidation of agricultural holdings and the provision of better village communications and of other amenities designed to build up a corporate life in the rural areas.

#### ANNUAL REPORT OF THE ALL-INDIA INSTITUTE OF HYGIENE AND PUBLIC HEALTH, CALCUTTA, 1939

The annual report of the All-India Institute of Hygiene and Public Health for the year 1939 reviews modern trends in the training of public health officers. These trends are based upon the marked amplification that has occurred in the past 20 years in the concept of public health, originally limited to the prevention of infectious diseases and in the control of environment.

Current thought is increasingly, throughout the world, attaching a much wider significance to the functions of public health. These now imply a study and control of *all* factors which affect the health of the community. Medical measures alone are insufficient to ensure that the community has or attains a normal standard of health.

The physical effects of occupation and of housing, the nutritive value of the food available; social customs, the educated consciousness of the community to attain a normal standard of health; economic

factors; these are some of the considerations which have to be studied in addition to the application of purely medical measures. Even the previous negative outlook of the purely medical measures is now becoming increasingly superseded by positive measures for the maintenance of health.

The function of investigation and training in public health is described as 'the development of the most efficient and practicable methods of scientific medical protection through organized community effort and the provision of opportunity for students to train themselves in the principles and application of those principles and methods'.

For the provision of opportunity to the students to train themselves and for a study of all the factors covered by the term public health, the necessity for the inauguration of 'controlled areas (to permit exemplification of methods) of a size sufficient to provide quality and quantitative facilities for students' self-participation' is emphasized. 'The principles determining the controlled community fields in public health correspond exactly to those governing the provision of a teaching hospital to a medical college presenting investigative facilities and quality and quantity standards for students' self-participation'.

Research in public health has been defined as 'the development of the most efficient and practicable methods of scientific medical protection through organized community effort'. Here again the necessity for controlled community areas is emphasized and the deficiency in the present organization of the institute in this respect is pointed out. 'The absence of controlled community fields places the institute under the same disabilities as would be faced by a department of clinical medicine in undertaking research in the absence of a teaching hospital. . . . The result has been that it has not been possible for the institute to discharge its chief function of making contribution towards the demonstration of the *utilization* of scientific knowledge in the advancement of community health.'

Having defined the primary function and scope of an institute of hygiene and public health in the matter of teaching and research, the report goes on to mention the deficiencies in the present organization of the institute and the curriculum and training. Special regard has been paid to the definite requirements of this country in determining the line of re-organization.

'Public health is organized community effort for medical protection, and, as such, is social medicine, the utilization of which must be different under varying social-economic conditions even although the principles derived chiefly from medical biology are universally similar. Consequently, it is essential that organization for instruction and research must vary from country to country during the levelling up process. Malaria must be afforded an importance in India that would be uncalled for in England. Health insurance cannot be given the same prominence in China as in Germany.'

An account is given of the progress made in the introduction of reforms in the training of public health officers and mention is made of the proposals under consideration for bringing the All-India Institute up to a standard comparable with similar institutions in other and more advanced countries.

The report goes on to say: 'The D.P.H. training should be one of the first educational fields to demonstrate the greater demand for local qualifications in the light of local variabilities in administrative practices. This recognition will be accorded shortly after the students are given adequate practice locally under Indian community conditions'.

#### APPENDIX TO THE REPORT OF THE CHEMICAL EXAMINER TO GOVERNMENT, PUNJAB, FOR THE YEAR 1939

[As usual, Lieut.-Colonel Thomas has an interesting appendix to his report which we think will be of more value to our readers than a résumé of the activities of the department therefore we reproduce it in full.]

## APPENDIX—

*Chemical warfare*

With the rapid progress made by modern aircraft in speed, range, carrying capacity and ceiling height, a war amongst so-called civilized nations can directly affect their civilian population, in other words, the civilian as well as the soldier must be prepared to face courageously and intelligently the shock of military attack.

The nature of such an aerial attack may be by any or all the three following types of bombs:—

- (1) High explosive.
- (2) Incendiary.
- (3) Gas.

In reviewing the effects of an aerial bombardment on a civilian population, our most recent and reliable knowledge is from the civil war in Spain which ended in 1939. No detailed information is so far obtainable of the Russian air attacks on the Finnish towns or of the German aerial bombardment of the Polish towns except that gas is not being used. Gas was not used in Spain nor is it being used in China, but there is proof that gas was employed latterly in Abyssinia in order to expedite operations before the setting in of the seasonal rains.

I cannot, therefore, do better than quote freely from a pamphlet on 'Lessons from Barcelona' by a Major MacRoberts who was present at some of the bombardments on that city.

*High explosives*

'The type of high explosives which has been used with most devastating effect in Spain is a percussion bomb bursting on impact. Made of light metal in weight from 100-250 kilograms, it has no serious crater effects; in many instances the craters were but a few inches in depth, but the blast effect has been such as to demolish the walls of a building in a lessening degree to a radius of as much as sixty yards from the point of explosion.

On the other hand, the important, and from our point of view, the vital fact to remember is that the pressure waves—the blast—only radiates over the surface of the ground from a percussion bomb. There are no violent underground tremors—no seismic effects. The damage is all above ground, hence the supreme importance of underground shelters. Underground we are safe, and a seven-foot deep trench in our backyard is just as effective, and probably more so, than a great strongly constructed basement shelter, because in any form of cellar or basement accommodation there is the additional factor to be taken into consideration of the ability of the roof of the basement to support the weight of the total collapse of the building overhead, and under the very worst conditions the total concentration of a load may reach a maximum of two tons per square yard.

The other type of high explosive bomb which has been used with varying success in Spain is what is known as the armour-piercing delay-action bomb. It must be admitted that the direct hit of an armour-piercing bomb presents an almost unanswerable problem. But there again is one of its chief drawbacks against its general use. It must be a direct hit—a miss is as good as a mile; it is so entirely local in its effect. And unless there is a direct hit on a shelter there is none of the terrifying blast effect which is connected with the percussion bomb.

Let it suffice for us to say that although there is no protection from the direct hit of a missile of this type unless there is overhead protection of at least twenty feet of solid earth and rubble, or fifteen feet of concrete, nevertheless there are so many factors militating against its general employment in attack against a civil population that it may be assumed that it would only be used in any great numbers against targets of supreme military importance.

The effectiveness of an armour-piercing bomb lies in its penetrability, and to achieve this its stream-lined shape, its sharp-pointed highly-tempered nose cap, its rather complicated delayed action fuse, and its great

weight of solid steel which may vary between 1,000-2,000 lb., all combine to make it a most costly projectile to manufacture.

The armour-piercing bomb relies for its power of penetrability on its great weight alone. The force of gravity draws it down to tear its way through any obstruction save the most heavily protected armour or earth-works. It is like a projectile hurled from a 15-inch naval gun. It is, in fact, almost the same type of armour-piercing shell. The armour-piercing bomb is equipped with a delayed action fuse which is usually placed in its base. The fuse ignites the explosive charge after the resistance of the earth has brought the huge weight of metal to a final halt. By means of its shape and pointed nose it is enabled to bury itself deep in the ground to a depth of ten feet or more according to the material resistance offered by earth or concrete. The explosion then occurs, and a great yawning crater varying from ten feet to fifteen feet in depth is hollowed out at the point of impact—a mass of debris being thrown up in all directions, i.e., the "splinter" effect referred to in textbooks. It will be seen, therefore, what a problem our engineers are faced with in constructing underground shelters which will withstand the shock of a direct hit from such a force. And yet again, if we study its effects it will be seen that there are very definite limiting factors. I placed the greatest importance on its entire absence of lateral blast effect—for unlike the percussion bomb, which radiates over the surface, the blast of an armour-piercing bomb is smothered or muffled by its own crater effect'.

Casualties in such cases are due to—

(1) People being trapped by falling masonry or injured in resulting fires.

(2) *Blast*.—Casualties are picked up dead, without apparent wounds, and only showing blood-stained fluid trickling from the mouth or nose. Post mortem the lungs are found to be torn.

(3) *Flying glass or fragments of the bomb*.—During the Dussehra bomb explosion of 1924, I myself was present at a post-mortem examination on one of the victims. A tiny fragment from the casing of the Mill's bomb was found in the body but this small fragment which had been projected with such velocity had completely reduced the whole liver to pulp resulting in immediate death.

*Incendiary bombs*

Modern chemistry has brought incendiary technique to a new stage. As a result of the invention of aluminothermy incendiary bombs have attained such an importance that they appear to be very dangerous weapons for bombarding towns, petrol tanks, gasometers, stores, ammunition dumps, etc., taking also into consideration the fact that a bomber can carry large quantities of such bombs. Some years ago there was a wave of incendiarism in Lahore. Some students made various attempts to burn letter-boxes. Phosphorus dissolved in carbon bisulphide was the combustible chemical generally used. The Thermit and Electron-Thermit incendiary bombs in contrast to phosphorus burn independently of the oxygen contained in the air. These bombs have the property of what is known as 'sub-surface persistence' and can burn at an initial temperature of 3,000°C. Such bombs are usually small, weighing from 2-4 lb., so a big bomber can carry upwards of 2,000 such bombs which can be scattered indiscriminately over cities and start numerous fires. An efficient Fire Brigade is the best protection.

Casualties in such cases are due to—

- (1) Burns.
- (2) Shock.
- (3) Sepsis.

It has been reported from Spain that shock caused the greatest number of fatalities in such cases and that the most successful treatment against shock was blood transfusion. As blood donors women were better volunteers than men in the proportion of 4 to 1.

The recent book on the treatment of wounds caused by high explosives and burns is 'Medical Organization and Surgical Practice in Air Raids' by Mitchiner and Cowell, published in 1939 by J. & A. Churchill, price

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## ABDOMINAL POST-OPERATIVE DRESSING

A sterile dressing is applied to the abdominal wound followed by a piece of an 'Elastoplast' bandage, sufficiently wide to cover completely the sterile dressing and sufficiently long to stretch from one side of the abdomen to the other.



Piece of 'Elastoplast' Bandage showing centre portion rendered NON-adhesive by dabbing with cotton-wool.



Section showing 'Elastoplast' applied over a sterile dressing.



Section showing 'Elastoplast' cut up centre and turned back for examination and re-dressing of wound. Fix with clip or safety-pin.

The centre of the 'Elastoplast' is dabbed with cotton wool, thus rendering it non-adhesive, to an extent that will just cover the sterile dressing. This is then applied to the abdomen with the required tension, so that the non-adhesive portion covers the dressing.

When it is desirable to change the dressing the following procedure is necessary:—

The centre is slit up with a pair of dressings scissors; the sterile dressing is changed and the cut ends are folded back over the dressing and fastened with a clip or safety-

pin. For subsequent dressings it is then only necessary to unfasten the clip or safety-pin for the wound to be examined and re-dressed.

Where frequent change of dressing is required, an improved method is illustrated below.



Completed Dressing.



Dressing opened for inspection.

(1) Rods. (2) Strips of 'Elastoplast' folded round the rods, so that the adhesive surface does not come in contact with dressing. (3) Rubber bands. (4) Dressing.

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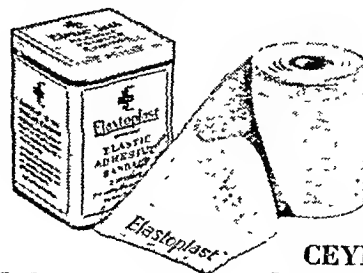
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half a guinea. (Reviewed in the July 1939 issue of the *Indian Medical Gazette*, p. 442.)

#### Gas

From about 3,000 chemical poisons which were closely examined both before and during the Great War by the belligerent states with regard to their suitability as fighting materials, *i.e.*, for use in open country, only about 20 were considered to be of any practical use. The reason for this small number lies in the very high requirements exacted of these materials, such as immunity against the oxygen of the air, atmospheric and terrestrial humidity, indifference towards the material of the projectile, resistance to detonation, intensity of the physiological effect, large volumetric weight in gaseous form, etc., to which may be added special properties, according to the application (defensive or offensive materials). These explanations will, at the same time, explode the myth of the existence of new secret discoveries exerting a more deadly effect. It may happen that one or the other material may still be found to be suitable. Yet the demands which must necessarily be made on its properties will naturally limit the probability that it would be more effective than those already known (Kinttoff).

The object of poison gases is to disable or kill the opponent. Therefore, their effect is directed to various parts or organs of the human body according to which they are classified as follows:—

- (1) Eye irritants.
- (2) Nose and throat irritants.
- (3) Lung irritants.
- (4) Vesicants or blister gases.

The lung irritants and the vesicants are the most important groups. Phosgene is a typical example of a lung irritant and mustard gas is a true vesicant.

An excellent book by Lieut.-Colonel Bilderbeck, *R.M.S.*, called *A. R. P. Instructors' Manual*, price Rs. 2-4-0 and published at the *Times of India Press*, Bombay, gives all the symptoms, treatment, etc., of poisoning due to the war gases together with such information as is useful to us in India. I am recommending this book to anyone who is interested in this subject.

#### Conclusions

The odds are that gas is not likely to be used against civilians, even untrained civilians, as so much more material damage can be done by high explosives and incendiary bombs. The providing of respirators does not appear necessary at present. Equally effective protection can be obtained by remaining quietly indoors. During the Great War the French and Belgium peasants in the forward areas were not supplied with respirators. When a gas attack was made they left their fields and shut themselves up in their houses and suffered little, yet they must have been in a much higher concentration of gas than any civilian population is ever likely to be.

In an air raid it is certain that if poison gas were used, the initial attack would consist of high explosive bombs. Such an attack would have the effect of loosening the fabric of a building above ground and thus permit the infiltration of poison-gas in a subsequent attack.

As a famous instructor has stated at one of the Home Office A. R. P. Schools: 'If you want to get at the sardines you have first to open up the tin'. A high explosive bomb is only a high explosive shell in a different form, for whereas one is propelled from a gun, the other is dropped from the sky, and every soldier knows that the only protection from shell-fire is in a trench.

Public psychology is an increasingly determining factor in modern warfare. The threat of air attacks against the civil population constitutes an important psychological weapon which an unscrupulous enemy may employ.

If the present war continues or spreads to other countries, the subject of chemical warfare will be dealt in much greater detail in our next year's report.

### ANNUAL REPORT OF THE CHEMICAL EXAMINER TO GOVERNMENT, UNITED PROVINCES AND CENTRAL PROVINCES, FOR THE YEAR 1939

ONE THOUSAND SIX HUNDRED AND FIFTEEN medico-legal cases and 5,613 articles were examined during the year under report as against 1,524 cases and 4,970 articles in 1938.

The total number of human poisoning cases examined under this head was 413. Poison was detected in 60.5 per cent of cases as against 67.0 for 1938.

Dhatura was again the most commonly used poison. It was detected in 37.5 per cent of the cases.

Opium, arsenic, mercury-salts, aconite, nux vomica (strychnine), cyanides and alcohol came in order of frequency forming 23.5, 18.6, 3.7, 3.0, 2.3, 1.9 and 1.1 per cent respectively of the detected poisons. In 2.3 per cent of cases unidentifiable organic poisons were found. This shows the need for research on the indigenous vegetable poisons. Bones and ashes of five persons were received and examined during the year. Arsenic was found in four of the cases.

Thirty-six cases of animal poisoning were examined compared with 23 cases for the preceding year. The percentage of detection was 66.6 compared with 65.2 for the year 1938. Arsenic was detected in 14 of these cases. Kancr came next in order of frequency.

One thousand one hundred and sixty-two stains were examined comprising 853 blood stains and 309 blood and semen stains (sodomy and rape cases). There has been a considerable increase in the number of murder cases during the latter part of this year.

### CHEMICAL EXAMINER'S DEPARTMENT, GOVERNMENT OF MADRAS: REPORT FOR 1939

THE total number of articles examined in the chemical examiner's department increased from 8,913 to 9,392.

Four hundred and fifty-eight cases of human poisoning were examined as against 467 in the previous year and poison was detected in 54.6 per cent of the cases. Some of the cases described below show how an ignorant or a mistaken use of certain drugs, some of which are regarded as medicinal, ended in disastrous results and they should serve as a warning to the general public.

A religious mendicant sucked perchloride of mercury mistaking it for alum and died of the effects of poisoning. Another gave a paste containing datura to a husband and wife to enable them to travel without fatigue. The husband, who ate a large quantity of the substance, lost consciousness and when he regained consciousness the next day, he found that his wife had been throttled to death. A shopkeeper sold denatured spirit to a woman mistaking it for 'omam water' (caraway water). The ignorant woman administered it to her child with fatal result. Two children were given the bark of *Holarrhena antidysenterica* Wall (*Kurchi* or *Coness*) as a purgative with fatal results to both. A young man accepted a bet and ate yellow oleander kernels. He was removed to a hospital in a collapsing condition where he recovered. Another was given toddy with mercury by a quack, to cure him of an evil habit. He became seriously ill, but recovered under hospital treatment. Investigation of a suspected case of poisoning of a hysterical young girl of twenty resulted in the discovery that she had been beaten to death by a magician who had offered to drive the devil out of her.

There was a slight reduction from 26 to 23 in the number of animal poisoning cases. Poison was detected in 56.5 per cent of the cases. Arsenic and oleander account for the largest number.

The number of stains examined increased from 979 to 993. Blood was detected in 91.8 per cent of the blood-stain cases. The examination of such cases has been of great assistance in the investigation of crimes and prosecution of criminals.

Miscellaneous medico-legal cases involving the examination of firearms, bullets, bones and tissues, counterfeit coins, re-used stamps, documents, etc., increased from 99 to 136. One of the noteworthy cases is that of a village officer who was entrusted with the

duty of conducting an election to a *panchayat* board and who was alleged to have tampered with the notice of election by altering the day and date of election. An examination of the document under the microscope and in ordinary and ultraviolet light, proved that the allegation was true.

One hundred and twenty-five cases were examined for Government departments, as against 214 in the previous year.

#### REPORT OF THE EUROPEAN MENTAL HOSPITAL AT RANCHI FOR THE YEAR 1939. BY MAJOR MOORE TAYLOR, M.D., D.P.H., I.M.S., MEDICAL SUPERINTENDENT

THE condition of every patient on admission is thoroughly investigated, the routine consisting of a complete physical, pathological and psychological examination. This is followed by dental and ear, nose and throat, and where indicated, ophthalmic examination. Thereafter treatment is prescribed, and all patients are given the benefit of whatever special treatment is indicated. The treatments now in common use are cardiazol shock-therapy, prolonged narcosis, malariotherapy, pyretotherapy, hydrotherapy, occupational therapy, in addition to whatever physical, medicinal or endocrine therapy may be called for in individual cases. Shock-therapy is expensive, highly specialized and takes three or four months to complete in any one case, but its results are encouraging, and in the present state of our knowledge it offers the only hope of cure or amelioration in certain cases of schizophrenia. In spite of the difficulties and dangers of the treatment it has justified itself as a form of therapy. Treatment by prolonged narcosis is found particularly useful in states of excitement and especially in the manic-depressive psychoses. Hydrotherapy is an important form of treatment in many types of mental disorder and is used extensively in this hospital. The detailed technique of all methods of treatment has been dealt with in previous annual reports of the hospital, and repetition is, therefore, unnecessary.

Occupational therapy continues to be one of the main features of the hospital. The average number of patients employed in useful tasks in the hospital represents over 80 per cent of the population. All nursing sisters are now fully qualified to supervise this treatment, either in the occupational therapy department or in the wards. The crafts taught on the female side include crochet, tapestry, painting, leather work, embroidery, quilting, plain sewing and mending, dress-making, tailoring, basket-work, raffiawork, knitting of all types, bead-work, etc.; and on the male side carpentry, book-binding, upholstery, cloth-weaving, rug and mat making, basket-work, paper bag making, decorative paper work, picture-framing, metal work, etc. Most of the articles made in the department are utilized in the hospital but any surplus stock is sold to the public. During 1939 the female occupational department undertook all the tailoring and dressmaking required in the hospital and in addition sold goods to the value of Rs. 396-7-0, an increase of Rs. 97-3-6 compared with last year, while in the male section all manufacture of furniture, repairs to hospital furniture and plant were executed, and goods sold to the value of Rs. 423, an increase of Rs. 57 compared with last year.

Classes in physical drill, folk-dancing and games are held daily, and the patients, assisted by the staff, staged a number of excellent concerts during the year. Parties attended the cinema at Ranchi whenever suitable films were shown. The usual social evenings and dances continue, and a full Christmas programme was brought to a close with the usual fancy dress ball. The cricket, football and hockey teams played a number of friendly matches on the hospital grounds, and also at Ranchi, some of which they won.

In the treatment of mental illness it is extremely important that as far as possible, the patient should not feel that his (or her) liberty is being unduly interfered with. There are no locked doors in the hospital, and patients are allowed to write and receive

as many letters as they wish, and it is a rarity for any letter written by a patient to be withheld, indeed, most of the correspondence remains uncensored.

Voluntary boarders who elect to manage their own affairs are permitted to do so.

During the year a thorough investigation into the dietary scale was carried out, and a report was submitted to the managing committee. The aim has been to set up a standard by which each patient should receive his physiological proportion of calories and vitamins at the least possible cost, and to provide a certain amount of variety. It has to be conceded that the dietary, considering all circumstances, is an excellent one—and perhaps more elaborate than that which can be obtained by many of those who have to pay the rates and taxes. The answer to this is (1) that diet is one of the most important methods of treatment, (2) the better the diet the greater is the hope of recovery and (3) the higher the recovery rate, the less will be the contribution charges payable by Governments. Nevertheless the average *per capita* cost under diet for the year 1939 has been reduced to Rs. 280 per annum.

It is gratifying to be able to report that all uniforms of ward-boys and ayahs, and all garments and clothing for both male and female patients have been made in the female occupational department. In former years a substantial part of this work had to be undertaken outside the hospital. This is the first year that the entire requirements have been met within the hospital, and for this, the credit must go to Sister Haagensen, who has held charge of the female section of the occupational department throughout the year under report.

#### ANNUAL REPORT OF THE PUBLIC HEALTH DEPARTMENT IN THE CENTRAL PROVINCES AND BERAR FOR THE YEAR 1938

THE state of public health during the year was unsatisfactory. The death rate was higher by 7.95 per mille than the mean of the previous five years and exceeded that of the previous year by 8.44 per mille. The infant mortality rate was 19.60 higher than in 1937 and exceeded the mean of the five previous years by 12.07. The increase in mortality occurred under all heads with the exception of plague, smallpox and injuries.

Owing to the serious outbreak of cholera, the ordinary routine public health and medical relief work of travelling dispensaries and even of stationary rural dispensaries was greatly disorganized as all efforts were concentrated on the suppression of cholera. This was reflected by a general deterioration in health. The chief causes of increase in mortality compared to the previous year were: cholera (44,225), malaria (34,662), respiratory diseases (8,619), diarrhoea (7,896), and other fevers (5,383).

The urban and rural death and infant mortality rates exceeded those for 1937 by 7.69, 8.53, and 20.12 and 10.53 respectively.

Four tuberculosis clinics, one each at Nagpur, Jubbulpore, Amraoti and Raipur, were established during 1938. Five thousand, two hundred and seventy-seven patients attended at these clinics. Of these, 1,365 were found positive to tuberculosis. Total number of sputum examined was 3,000, of which 632 were found positive. Four thousand and eighty x-ray examinations were made and only 1,593 gave positive signs; 1,515 pneumothorax operations were performed. Number of deaths amongst patients who attended the clinics was 59. One thousand and eighty-two patients ceased to attend. Two thousand five hundred and ninety-one cases were visited and advised at their homes.

Guinea worm is specially prevalent in Damoh subdivision of Saugor district which abounds in step wells. Efforts to get these wells converted into draw wells have so far failed.

*Leprosy*.—The number of deaths from this cause was 1,579; 255 more than last year. The disease is prevalent all over the province.

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---

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\**B.M.J.*, 1937 August 28. Page 412.



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During the year, two more leprosy clinics were established at Bhandara and Arni (in Yeotmal district), making a total of 37 centres. The number of sub-centres remained the same, *viz.*, 51.

Systematic resurvey and active propaganda was carried out, resulting in the discovery of 409 new cases which were brought under treatment.

There are in the province 11 assistant surgeons and 18 assistant medical officers and 16 private medical practitioners, who have received special training in leprosy at the School of Tropical Medicine, Calcutta.

During the course of their tours sub-assistant health officers of Chanda, Bilaspur, and Drug came across 255 cases of yaws. All these cases have been brought under treatment.

There were 6,539 deaths from child birth, of which 953 were registered in municipal and other towns and 5,586 in rural areas. This corresponds to one maternal death to every 84 urban and 107 rural births, including still births. The general, urban and rural maternal death rates are 9.64, 11.86 and 9.34 per 1,000 births, including still births, respectively.

### TRIENNIAL REPORT ON THE WORKING OF THE HOSPITALS AND DISPENSARIES IN ORISSA FOR THE YEARS 1936, 1937 AND 1938

THE Province of Orissa was created on the 1st April, 1936. The province had, on the day of her creation, 176 hospitals and dispensaries which are by no means considered sufficient for the medical needs of the province. During an inspection of hospitals and dispensaries in the province it was noticed that many of them under the management of local bodies were not in as an efficient condition as they should be, especially those in the agency area. As regards hospitals, it may be said that most of them are poorly equipped and medical, nursing, and menial staff are inadequate for the number of patients each hospital has to deal with. There is a further deterioration in these respects in many institutions as payments of contributions by local bodies are often in arrears and do not suffice to meet the expanding demands. The progress in effecting improvements of the hospitals and dispensaries was slow owing to requisite funds not being always forthcoming. Local bodies, as proprietors of class III hospitals and dispensaries, have placed the management of the institutions with managing committees constituted with local members with the idea that they should endeavour to make the institutions self-supporting by raising local subscriptions and to relieve the boards thereby of a large proportion of the recurring expenditure which they could utilize in extending medical relief to other areas. With a few honourable exceptions, these committees function in name only and evince little interest in the institutions. They also do not appear to realize the civic responsibility for improving the institutions under their management so as to render better medical facilities to the poor for whom the institutions are primarily meant. Such being the state of affairs in the management of hospitals and dispensaries under the local committees, they have not been able to create public feeling for regular contributions towards the upkeep of the dispensaries, thus defeating the purpose for which such committees were established.

Since the formation of the province a great impetus has been given to the progress of medical work in the province as a whole. There have been visible signs of greater activity in almost every direction and in all that concerns the welfare of the medical institutions in the province. There has been a general awakening amongst all who are interested in medical work which, it is hoped, will lead to better results in future. The popularity of the scientific and modern system of medicine, especially in the agency area the inhabitants of which are somewhat averse to medical treatment, has been kept always in view and measures are being taken in that direction. All such improvements which have been possible during this short period are due to the wise liberality of Government, who have not only

contributed in a large measure to ameliorating the sufferings of the poor people but have also stimulated public interest and benevolence.

### THE PREMANANDA FREE CHARITABLE OUT-DOOR LEPRO DISPENSARIES, CALCUTTA. ANNUAL REPORT FOR 1939

During the year 905 new patients were admitted at Maniktola and 260 at Kalighat. This is an increase of 274 on last year.

The total number of patients who attended for treatment during the year was at Maniktola 1,405 ordinary patients and 200 street beggars, who are classified separately, and at Kalighat 533, and 71 beggars.

These made 33,967 attendances at Maniktola and 11,152 at Kalighat. Last year's figures were 27,438 and 12,039.

Of these patients 633 (Maniktola) and 294 (Kalighat) attended sufficiently regularly to justify re-examination at the end of the year. The following results were obtained:—disease arrested 110; much improved 416; slightly improved 278; the same 118; worse 5.

One of the members of the dispensary staff is employed as part-time visitor to the homes of patients who have discontinued treatment, to explain to them the serious nature of the disease, to persuade them to return to treatment and take the necessary precautions against the spread of the disease. He paid 411 visits; 80 patients were traced, and of these 49 returned to treatment; 48 were found to have given wrong addresses; 2 had died; and of the rest no trace could be found.

We have appointed three whole-time clinical assistants in place of two whole-time and two part-time workers.

We have recently produced a pamphlet in Bengali containing instructions to patients on admission, explaining the nature of the disease, the principles of treatment and precautions to be taken. This will meet a long-felt need. A Hindi translation is being prepared.

In our report last year we announced our intention of rebuilding the Maniktola Dispensary. The plans had to be adapted to the very limited ground available. They provide for a large treatment room and smaller dressing room on the ground floor, and laboratory, office and store on the first floor. The expense has been met in part from the building fund, and in part by an anonymous donation from England, and the equipment of the laboratory by a grant of Rs. 2,000 from the Government.

The commencement of the building operations in November was the occasion for the outburst of opposition from certain neighbours; this led to police court proceedings which held up the building for another three months. Happily the efforts to obstruct the work proved futile and now the building is well in hand and should be finished by the end of April 1940. These new quarters will very much add to the efficiency of the Maniktola Dispensary.

Our next task must be to improve the premises at Kalighat.

The Calcutta Corporation without any warning reduced their grant from (1938-39) Rs. 8,000 to Rs. 5,000. We were therefore faced with a very serious situation. The situation was saved by the generosity of of the Trustees of the Crichton Trust who gave us a donation of Rs. 2,500 and by other kind friends. This has enabled us to pay our way in the current year, 1939-40, but, our mounting expenditure, due to the increasing work and the improvements introduced, will make it difficult to meet our bills in the coming year, unless the Corporation restore the grant in full.

Our first need is for a gradually expanding income that will meet the needs of the normal development of the work.

Our second need is for a capital sum to meet the cost of new premises at Kalighat.

Our third need is for friends who will co-operate in the struggle against this terrible disease. We are always grateful for gifts in kind, especially of bandages and cotton-wool which we use in large quantities, and of



food and cigarettes, which we give to our poorest patients, when the time for the Christmas feast draws near.

We hope that many who read this report will send their subscription to the Secretary, Premananda Out-Door Leper Dispensaries, 42, Cornwallis Street, Calcutta.

#### MEDICO-LEGAL SOCIETY, BIHAR, 1939-40

[WE have received the first annual report of the Medico-Legal Society, Bihar. It appears that this society was founded in April 1939. We give below an abstract from an appeal to join the society issued by the President, the Chief Justice of Bihar, as it expresses our own opinions on the subject. It would be an advantage to other provinces of India if they followed the lead given by Bihar and formed similar societies.—EDITOR, I. M. G.]

A Medico-Legal Society has been started with a view to promoting medico-legal knowledge in all its aspects. It will consist of qualified members of the legal and the medical professions and such other persons as may be interested in the objects of the society. The need for such a society is obvious. Lawyers have often very little knowledge about the human system and frequently cannot fully appreciate the medical reports which are at times difficult and complicated and the medical men have an equally meagre idea about the legal problems arising out of their reports. The result is that a clear understanding of the problems becomes difficult. To promote justice a better understanding between the two professions is necessary not only for members of the two professions but also for the judiciary. The idea is to provide a common platform for all those who are interested in the problem to meet together, read papers on medico-legal subjects and discuss questions arising therefrom.

## Correspondence

### 'DOPING' IN ATHLETIC CONTESTS

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—It was with the greatest interest that I read Colonel Phipson's paper on 'doping' in athletic contests, in the August number of the *Indian Medical Gazette*. It is a subject towards the medical aspect of which very little attention has been paid; and yet, in view of the considerable increase in the practice of 'doping', it is a matter of the greatest importance that its effects should be fully understood, and its dangers realized. Colonel Phipson's warning in this respect is therefore timely, and should be widely appreciated. It is, indeed, surprising, that the matter has been hitherto so neglected, not only in view of its practical importance, but also on account of its undoubted novelty and attraction as a field of research.

What is 'doping'? If we confine its meaning to the use of drugs which are toxic, injurious, or dangerous, such as cocaine, benzedrine, or cardiazol, then there is no doubt that the practice should be stopped, medical grounds alone being sufficient warrant. In horse-racing, the Jockey Club deal with cases of 'doping' with the utmost severity, though this, of course, is more on account of the large sums of money involved, than any particular consideration for the horse. If, however, we use the term in its widest sense, to include any means adopted to increase one's athletic performance above its normal standard, it becomes increasingly difficult to decide where to draw the line. In this connection the paths of ethics and medicine may diverge, or coincide; and what in one case may be a comparatively harmless procedure, may, under different circumstances, be quite the reverse, either ethically, medically, or both.

Many sporting writers refer, in the words of Colonel Phipson, to the 'lofty standard of ethics, which, we presume, characterized the Olympic contests in the

golden days of Ancient Greece'. I wonder if this presumption is altogether justified. One cannot be too sure that there were not occasions when a 'swift' drachma or two were made by 'gingering up an outsider', or by 'nobbling' the favourite, which amounts ethically to the same thing.

Should one consider 'training', the usual preparation of an athlete for a contest, as 'doping'? Some of the lengths to which trainers go nowadays may well be considered to transcend the bounds of ethics, as judged by the highest standards. From the medical point of view, there is no doubt that judicious and intelligent training is advisable, to prepare the body for the approaching strain on its resources. But the over-trained athlete is a common occurrence. The Harvard crew, which won the Grand Challenge Cup at Henley in 1914, were said to have been trained to the pitch of hysteria, and some of the members burst into tears at the conclusion of the final.

When the Olympic Games took place in London in 1908, the Marathon race from Windsor to London was held on one of the hottest days of the year. Dorando, an Italian, was the first to enter the White City stadium; he was obviously exhausted, and as he neared the finishing line he collapsed. Some of his compatriots rushed on to the track, and threw a bucket of water over him. This partially revived him, and he attempted to get to his feet. In the meantime the next competitor, Hayes, an American, was entering the stadium. In the excitement that ensued, the Italian's friends lifted him up and pushed him forward, with the result that the gallant Dorando managed to stagger past the winning post before collapsing again. The Americans immediately lodged a protest on the grounds of unfair assistance, and the Italian was disqualified. This nearly finished him altogether, and he was carried to the dressing room practically unconscious. He was examined by the official medical officer who stated that his heart (presumably his apex beat) was displaced half an inch. His condition gave rise to the gravest anxiety, and he showed no signs of improvement until he was informed that Queen Alexandra had given him a special gold cup as a reward for his gallant effort, after which he slowly recovered. The point is this; the pluck and endurance which had carried him through that gruelling 26 miles would not have failed him in sight of victory, except as a result of complete and utter physical exhaustion. In this case, the 'dope' was merely a bucket of water externally applied, but the final effort made following its stimulating effect, might well have had an even more serious effect than it did.

Public opinion, I am afraid, is not altogether a reliable guide. A competitor might openly, and in full view of the spectators, swallow a couple of benzedrine tablets, without exciting much comment. But let his trainer approach him with a few cubic centimetres of glucose solution in a syringe, and in all probability the Riot Act would have to be read.

'Doping' should undoubtedly include psychological stimulation. The shouts of his supporters, or a man's own determination, which spur him on to further effort in spite of his fatigue, are just as dangerous in this respect, as a drug which diminishes the feeling of fatigue; and what of the Christian Scientist (I have recently seen one in action), who refuses to acknowledge the symptoms of fatigue! Propaganda and the 'war of nerves' are 'dopes' very much employed, especially in boxing, both as a support and encouragement, and also as a means of demoralizing or intimidating the opposition. Descamps, manager of Carpentier, was an adept at this form of ringside strategy. An interesting article by Gene Tunney, ex-heavyweight champion of the world, recently appeared. It was entitled 'Courage is a business', and in it Tunney endeavoured to show that the business side of professional boxing can not only get a man into the ring in spite of his 'funk', but can actually overcome it, and develop in him a true fearless courage; and he cites examples among many famous boxers to prove his contention.

With regard to some of the other means of 'doping' carbohydrates, in some form, have long been used, to





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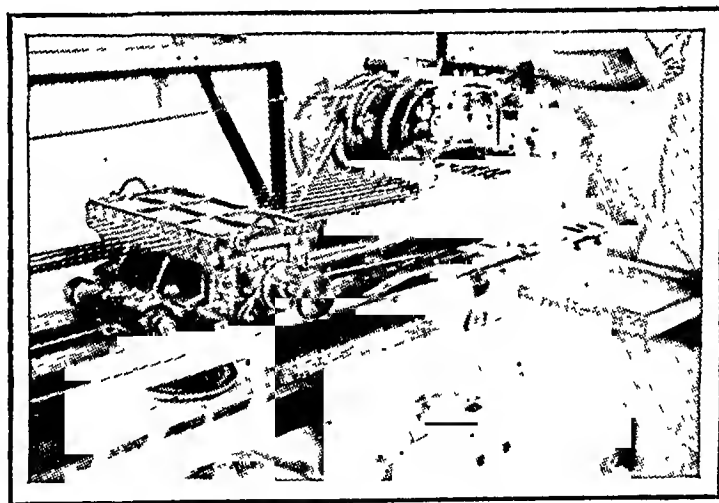
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defer exhaustion and to furnish a source of energy. I agree with Colonel Phipson, however, that it should be administered during the period of exertion. 'Premedication' with glucose is not likely to be of much use, unless the glycogen reserves of the body had already been depleted. The method would therefore appear to be of most use in long distance events, or other endurance contests. Some years ago, a South African farmer, Norton, arrived in England, and proceeded to break various long distance running records, such as London-Bath and London-Brighton. According to the press, he was considerably aided in this by a 'magic drink', which he took at intervals during his running. This drink turned out to be a solution of sugar in lemonade, and it is a fact, that this man, who was, I think, over 40 at the time, did put up some remarkable performances on the road.

The cutting down of the salt intake in an athlete's diet is generally done in an attempt to reduce weight. Surplus fat is in most cases undesirable and an unnecessary burden to an athlete. But 'wasting' can be carried too far, and, if persisted in, may have definitely harmful effects. The practice is particularly common among jockeys and boxers, whose weight has to be kept within certain limits. The method usually adopted is 'sweating' (Turkish baths, violent exercise in sweaters, etc.), and 'drying-out' (limiting the fluid intake). Jockeys and boxers both start young, and a deliberate and persistent refusal to allow the body to develop along its normal lines is bound to have an ill effect after a time. One of the most celebrated jockeys of all time, Fred Archer, is said to have ruined his health by continued wasting. The so-called classic races of England are run at 9 stone, but to be of general use throughout the season a jockey has to be able to ride at about 8 stone. He may have commenced his actual racing career at about 14, well within the weight limit then, of course. But while his skill and experience are growing, so also is his body, and when, after a few years, he is on the threshold of becoming a successful jockey, he is faced with the necessity of wasting for the rest of his career. Boxers, especially among the lighter weights, also start at an early age, and as they grow and develop they have to choose between entering a higher weight, with its tougher opposition, or wasting to remain in the same class; and many a boxer has fallen between the two stools. It is interesting to note that Jimmy Wilde and Gordon Richards, strong men of the ring and turf, respectively, never had to waste, and there is little doubt that their long and highly successful careers were due, in no small measure, to this fact.

'Oxygen-priming' under practical conditions is not of great value, as very little delay between its administration and the start of the race would be sufficient to restore the oxygen balance to normal. However, I did once see it put to an effective use, as follows: While holding a short service commission in the Navy, I was one of a batch of 'young doctors' sent to do a gas course. At the end of our training we were 'invited' to hold a quarter-mile race in gas masks. The field numbered about 20, and included several tough young midshipmen. However, as we lined up to receive our final instructions, one intelligent surgeon-lieutenant hooked his finger in the chin-piece of his mask, and got in about six good gulps of fresh unfiltered Hampshire air. Letting go at the 'Off', he streaked down the course and won in a canter. As he told me afterwards, he was clear of the field before he ever needed a breath!

I think everybody agrees that the disadvantages of alcohol far outweigh its potentialities as a source of energy. Nevertheless, it has its uses, and may be employed to allay an initial nervousness. For instance, the machine-like precision of the professional billiard player becomes almost subconscious as a result of constant practice. A 'quick one' before an important match might quite conceivably give him the initial confidence to get quickly into his stride, an important factor in these days of 2-hour sessions and 1,000 breaks! There is also the story of the long jumper who had developed a 'taking-off board complex', and was inches

short in consequence. Just before a contest someone gave him a nip of whisky, with the result that he forgot all about the board, and did a perfect take-off.

Artificial sunlight has become increasingly popular in recent years, but it is not without real danger. Cases have been reported of otherwise unexplained 'lighting-up' of foci of infection, particularly tuberculous, through injudicious use of 'artificial sunlight' lamps.

Benzedrine, as its stimulating properties became known to the public, began to be used fairly frequently, and at one Wimbledon was said to have been employed by certain players, not only to lessen the sense of fatigue, but also to speed up their sense of anticipation. The drug has, of course, since been brought under the scope of the Dangerous Drugs Act, which has fortunately made it less easily accessible.

The administration of hormones, such as testicular extracts, to normal healthy athletes might not prove an altogether unmixed blessing, particularly to trainers responsible for their teams. The effects, psychological and physical, might well spread beyond the immediate end in view. Some of the oestrous-producing substances used to alter the date of menstruation in women athletes have certain disadvantages. The results of their administration are often unreliable, and gastrointestinal disturbances are common. Also one cannot be altogether happy about disturbing the menstrual cycle in a woman whose pelvic physiology has hitherto functioned normally. It is surprising how little many of the women athletes of to-day worry about their 'periods'. Aerobic and tap dancing, and similar athletic features of modern stage technique, call for a considerable degree of physical fitness in their exponents, to carry them through a long run of repeated performances. Yet the young lady of the chorus rarely takes, or is allowed, a day off, on account of being 'unwell'. As a matter of convenience, the use of internally worn sanitary appliances has been widely adopted by women athletes, but the medical profession is still divided in its opinion as to their desirability.

With the temporary cessation of international athletics, the question of 'doping' can perhaps be relegated in favour of more pressing affairs. When, however, the present craze for mutual destruction has passed, and we can once more devote our attention to more healthy pursuits, there is no reason to suppose that the intensity of sport, especially as regards record-breaking and international contests, will not become as great as before. The question of 'doping' will then once again come to the fore, and the matter will have to be taken up. I would suggest an investigation by a committee of medical men (the profession has always included famous athletes in all branches of sport), who would lay their findings and recommendations before the various national and international athletic bodies. These in turn could then consider the necessity of legislation and control.

Yours, etc.,

W. J. MOODY, M.A., M.B.,  
F.R.C.S. (Ed.),  
MAJOR, I.M.S.

BRITISH LEGATION,  
KABUL,  
10th September, 1940.

## Service Notes

### HONORARY APPOINTMENTS

#### To be Honorary Surgeons to the King

COLONEL F. F. S. SMITH, V.R.S., 8th November, 1939, vice Major-General E. W. C. Bradfield, C.I.E., O.B.E.

Colonel E. G. Kennedy, 24th November, 1939, vice

Colonel S. G. S. Houghton, C.I.E., O.B.E.

Colonel R. H. Candy, C.I.E., 24th January, 1940, vice Colonel W. E. R. Williams, O.B.E.

*To be Honorary Surgeon to the Viceroy and Governor-General*

Colonel J. S. S. Martin, *vice* Colonel F. F. S. Smith, vacated 21st September, 1940.

**APPOINTMENTS AND TRANSFERS**

On reversion from foreign service under the Indian Research Fund Association, Major Jaswant Singh, an officer of the Medical Research Department, is appointed to officiate as Assistant Director, Malaria Institute of India, *vice* Major M. K. Afridi reverted temporarily to military employment.

On return from leave Major R. A. Wesson has been posted as Civil Surgeon, Meerut.

The services of Major V. Srinivasan, Civil Surgeon, Bilaspur, and Captain F. C. Leach, Civil Surgeon, Raipur, have been placed at the disposal of the Government of India Defence Department for military duty, with effect from 3rd September, 1940, and 1st September, 1940, respectively.

Captain T. M. Williams, Assistant to the Civil Surgeon, Poona, reverted to military duty, with effect from 8th September, 1940, forenoon.

The services of the undermentioned officers of the Indian Medical Service (Civil) are placed temporarily at the disposal of His Excellency the Commander-in-Chief, with effect from the dates stated against their names:—

Captain C. L. Greening. Dated 1st May, 1940.  
Major J. R. Dogra. Dated 2nd May, 1940.  
Captain T. Sommerville. Dated 2nd May, 1940.  
Captain I. J. Franklen-Evans. Dated 3rd May, 1940.  
Captain R. Passmore. Dated 6th May, 1940.

*Appointment*

The undermentioned officer retires with gratuity and is granted an emergency commission from the same date:—

Captain K. N. Rao. (Short Service Commission.) Dated 1st July, 1940.

**INDIAN LAND FORCES. INDIAN MEDICAL SERVICE  
(Emergency Commissions)**

*To be Lieutenants (on probation)*

Dated 1st August, 1940

Dwarka Prasad Puri.  
Rama Shankar Saksena.  
Cherukuri Venkaiah.  
Manchambhotla Ramarao.  
Perilakalathil Chandrasekharan Nedungadi.  
Kunhithyil Panayamparambil Anandan.  
Muhammad Yusuf Qureishi.  
Kanwar Moti Singh.  
Som Nath Sharma.  
Heera Lal Sah.  
Freedon Piroshaw Gazdar.  
Satyendra Prosad Mukherjee.  
Ajit Nath.  
Harold Anthony Davidson.  
Rajindar Singh Dhillon.  
Ram Krishna Satija.  
Nawab Ahmed Kuraishy.  
Manoranjan Das Gupta.  
Ambat Gopala Menon.  
Chuni Lal Chadha.  
Harbans Lal Anand.  
William Gregory Aranha.  
Laxman Babaji Belkhole.  
Bharat Mitra Saigal.  
Partap Chandra.  
Sudhir Chandra Roy.  
Nripendra Chandra Chatterjee.  
Nandkishore Ganesh Gadekar.  
Abdul Qadir.  
Ajit Kumar Gupta.  
Narendranath Dutt.  
Minoo Rustomji Vesuna.  
Gyan Chand Chawla.  
Mohammad Alam.

Dated 2nd August, 1940

Puthenparampil Oomen Oomen.

Kali Charan Chaudhuri.  
Sailes Chandra Banerjee.  
Sailendra Mohan Das.  
Sudhir Kumar Roy.

**LEAVE**

Lieutenant-Colonel C. J. Lodge-Patch, M.C., Medical Superintendent, Punjab Mental Hospital, Lahore, who was on leave *ex-India* till the 18th October, 1940, has been granted, by the High Commissioner for India, a further extension of his leave by 4 months from the 19th October, 1940, to the 18th February, 1941.

Lieutenant-Colonel M. Das, M.C., Superintendent, Alipore Central Jail, is allowed leave on average pay for 1 month from the 17th October, 1940.

Major B. M. Rao, Medical Officer, Meshed, an officiating Agency Surgeon, is granted leave for 2 months, with effect from the forenoon of the 9th September, 1940.

**RETIREMENT**

Lieutenant-Colonel N. K. Bal, M.C. Dated 10th September, 1940.

**PROMOTION**

*Major to be Lieutenant-Colonel*

J. L. Donnelly. Dated 25th September, 1940.

The seniority of the undermentioned officers in their present rank is antedated to the dates specified:—

Captain B. N. Bhandari. Dated 21st May, 1934.  
Captain B. L. Kapur. Dated 22nd May, 1934.  
Captain A. K. Dev. Dated 31st May, 1934.  
Captain M. Akram. Dated 2nd June, 1934.  
Captain M. S. Chadha. Dated 19th June, 1934.

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## Original Articles

### MORE NOTES ON CLINICAL HEART DISEASE

By GERARD KELLY, F.R.C.P.(I.)

MAJOR, I.M.S.

*Professor of Clinical Medicine, Medical College Hospitals, Calcutta*

#### *Some manifestations of elevated venous pressure in heart failure*

FIGURATIVELY speaking, the systemic veins may be regarded as a reservoir filled from the periphery by blood from the capillaries and emptied by the cardiac pump. Normally, the intake and emptying mechanisms are in dynamic equilibrium. The height of the venous pressure is a gauge of the fullness of the reservoir. When, in ordinary or in acute congestive failure, the right heart fails to empty the systemic veins, the venous pressure rises. This rise of venous pressure is reflected in the venous reservoir formed by the systemic and portal venous system behind the failing right ventricle.

*Engorgement of the liver.*—The hepatic veins enter the inferior vena cava at a considerable angle close to its point of entry into the right auricle. The blood flow in the hepatic vein is a feeble stream as compared with that in the inferior vena cava. The liver itself is a vascular sponge. In the early stages of failure of the right heart to empty the systemic veins, the liver holds back a considerable volume of the venous return. Storage of water within the liver cells is probable. Thus, enlargement of the liver may precede the rise and persist after the fall of venous pressure. In young people the liver capsule is more distensible and so as a rule in them liver engorgement is proportionately more marked than are the other signs of right-heart failure.

Engorgement of the liver is an almost invariable consequence of failure of the right heart. Very rarely right-sided failure, including liver engorgement, may occur in left-sided failure without the intervention of pulmonary engorgement, *i.e.*, in the absence of the usual evidence of left-sided heart failure, a phenomenon which, Harrison asserts, speaks against the idea that the overworked chamber is always the one to fail first. Most usually, however, liver engorgement is conspicuously absent in isolated left ventricular failure. We have the impression that the liver is sometimes slightly congested in peripheral circulatory failure of toxic origin. The remaining causes of liver engorgement are relatively infrequent. Occasionally, liver engorgement may afford early evidence of effusion into the pericardial sac, which by resting on the diaphragm about the vena caval hiatus may exert compression especially of the mouths of the hepatic veins,

which, as stated above, open into the inferior vena cava. Liver engorgement is disproportionately prominent in adhesive pericarditis because adhesions more readily kink the trunks and pinch the mouths of the hepatic veins than of the inferior vena cava. On rare occasions, a tumour mass may obstruct the proximal inferior vena cava or the hepatic veins themselves may become thrombosed.

A rare but interesting result of the increased venous pressure of right-heart failure is phleboscrosis of the hepatic veins, which is the analogue of sclerosis of the pulmonary artery in pulmonary hypertension. Cardiac cirrhosis accompanies some cases of hepatic phleboscrosis.

When right-heart failure is ushered in acutely, as for example by auricular fibrillation, hepatic pain and its associations may raise a suspicion of an acute abdomen. This suspicion may be heightened by the supervention of congestive vomiting. The pain is due to stretching of the liver capsule. Its localization is the right upper quadrant or the epigastrium: we shall refer presently to those cases in which pain and tenderness are localized in the epigastrium. The radiation of the pain is to the back, to the right scapula, and to the right shoulder (phrenic shoulder pain). A sharp or colicky character of the pain, local tenderness and rigidity, tympanites and the absence of any notable liver enlargement may further obstruct diagnosis. In the shock stage of coronary thrombosis such upper abdominal manifestations are not hepatic in origin: they occur reflexly from the sudden injury to the heart muscle or they are reflections of an attendant pericarditis, whilst the vomiting is probably due to a reflex from the heart through the afferent vagal fibres. The pain of acute engorgement, however, is usually of a continuous aching distressing type and is located in the right hypochondrium. It soon responds to digitalis and salyrgan. Provided the liver is not already cirrhotic, we initiate treatment with morphine gr.  $\frac{1}{4}$ . Leeching is a time-honoured remedy in these cases.

In chronic congestive failure the main burden of the patient's complaints is very often 'dyspepsia' or indigestion. In these cases congestion of the liver, of the stomach, of the intestines and of the pancreas produces slowness of digestion, anorexia, nausea, belching of gas, bloating of the stomach, a sensation of tension in the epigastrium and hypochondria, constipation, occasional bouts of diarrhoea, and rarely vomiting or bilious attacks. The patient may wonder where all the 'wind' comes from: 'vicarious respiration' is one answer, but not the correct one. In the tropics the possibility of a complicating amebiasis should not be overlooked.

The influence of the time factor in the production of the signs of right-heart failure is indicated by the following observations. The acute heart failure of diphtheria and of coronary



thrombosis may be attended within the course of a few hours by conspicuous liver engorgement and by but little or no œdema : the latter takes some days to develop. The practitioner should regard vomiting in diphtheria as an urgent symptom of impending circulatory collapse. Rapid and extreme liver engorgement in coronary thrombosis is, in Libman's opinion, highly suggestive of thrombosis of the right coronary artery. Septal infarction due to either right or left coronary thrombosis is commonly associated with high grade right-heart failure : an acquired interventricular septal defect murmur and liver engorgement may be prominent features of septal infarction, as in a recent case of ours. In an attack of paroxysmal tachycardia, the classical example of acute cardiac dilatation, downward bulging of the liver is detectable within a few minutes : with the abrupt fall of heart rate that marks the offset of the attack, the cardiac dilatation magically vanishes in a moment or two, while recession of the swollen liver is more gradual. A passing reference to acute heart failure is made elsewhere.

In his routine examination of the abdomen in a heart case the examiner should deliberately search for three important abdominal signs, namely, (1) enlargement of the liver, (2) enlargement of the spleen, and (3) ascites. He should invariably employ bimanual palpation for the detection of (1) and (2). In his quest for an enlarged liver, he should commence palpation in the right lower abdominal quadrant into which a Reidel's lobe may rarely wander. The swelling of the liver in engorgement is general and mostly downwards. Usually, the larger right lobe will be encountered projecting further down than the much smaller left lobe. Sometimes the engorged liver imparts to the palpating hand a definite impression that it is swollen, that its surface is convex and that its elasticity is increased. Ordinarily, the engorged liver feels smooth and firm; its lower border is rounded and feels thickened. In long-standing engorgement, the liver may convey the impression of hardness and its edge may feel sharp or obtuse. Tenderness at least of the liver edge is a usual finding, even in the absence of any complaint of pain. As a rule, tenderness is general over the hepatic region, *i.e.*, below the right costal margin and the epigastrium. Occasionally, pain and tenderness are localized over a small area in the epigastrium, and if in addition there is any suggestion of jaundice a misdiagnosis of gall-bladder disease is very likely. The degree of enlargement of the liver may be great or slight : generally the liver size waxes and wanes with the advance and retreat of failure. The associated *defense musculaire*, however, often prevents definition of the size of the engorged liver by palpation. In long-standing engorgement of the liver caused by heart disease, the overlying muscular rigidity usually disappears and little or no tenderness is

elicited on palpation. Confirmation of liver enlargement in heart failure should be sought by percussion of the liver in the middle line from the umbilicus to the ensiform cartilage.

In minor grades of failure, designated insufficiency of the right heart with early engorgement of the liver, the examiner may observe that as he exerts increasing pressure over the sub-hepatic area the cervical veins on both sides of the neck become more evidently engorged. Compression of the engorged liver empties it, as if it were a sponge, driving the blood via the inferior vena cava into the dilated right auricle with consequent visible and palpable cervical vein engorgement, which subsides when pressure is released, thereby permitting once more full expansion of the liver and descent of the diaphragm. This phenomenon, described in 1885 by William Pasteur of London, is called the hepato-jugular reflux. Expansile pulsation of the liver, especially of the left lobe, documents the advanced right-heart failure of long-standing mitral stenosis or of high-grade tricuspid disease. When one hand is applied over the liver anteriorly and the other is pressed into the right loin, this liver pulse gives the impression of an accordion expanding and contracting. 'When once the liver has begun to pulsate, it probably always continues to do so till death'—Mackenzie. Much more commonly the pulsation felt over the liver is not truly expansile, but is transmitted from the heart, particularly in cases of right ventricular enlargement or of aortic incompetence.

The engorged liver of right-heart failure commonly pushes the diaphragm upwards with some degree of resultant collapse of the right lung base. This is clinically evidenced by right basal dullness and deficient breath sounds and vocal vibrations. Such pulmonary collapse is distinguished from a pleural effusion by the fact that the upper level of dullness is not higher in the axilla than behind, and that in the prone position or in deep inspiration the increased dullness is notably lessened or become imperceptible. More appropriate to the occasion is the recognition of a right hydrothorax, in that hydrothorax is not only a further sign of congestive failure but is predominantly right sided.

In ordinary right-heart failure, the liver engorgement roughly parallels the rise of pressure observable in the cervical veins, except in the congested subject who is already suffering from cirrhosis of the liver. Venous pressure may be roughly measured by inspection of the cervical veins when these are easily observable. The retreat of the liver lags behind the decline of venous engorgement. In the first attack of congestion in the average case, digitalis and salyrgan produce a remarkably rapid retraction of the liver beneath the false ribs. In subsequent attacks of congestive failure the recession of the swollen liver under the same treatment is increasingly sluggish, the dyspepsia becomes more intractable and a sub-icteric tint



of the conjunctivæ develops. In protracted right-heart failure, the size of the liver may not decrease, in spite of marked subsidence of the signs of increased venous pressure. Peripheral œdema and transudation into serous cavities are usual but by no means invariable or proportionate accompaniments of liver engorgement in congestive failure.

The main causes of painful enlargement of the liver are congestion of the liver, amœbic abscess of the liver and cancer of the liver. Evidence of increased venous pressure, e.g., cervical vein engorgement, will be found *only* in the liver engorgement of heart disease: other cardiac symptoms and signs will of course be present here as well. In liver abscess, the signs of sepsis (spiky temperature chart, rigors, sweats, wasting, anæmia and leucocytosis: the latter may be comparatively slight or even absent) will point to the correct interpretation of the liver and right basal signs: any jaundice is latent: frank jaundice should suggest a complicating epidemic catarrhal jaundice, for example, as in a recent case of ours: the stools may show *Entamoeba histolytica* cysts: a previous history of dysentery or diarrhœa is sometimes helpful: radiography of the liver and a therapeutic test (emetine) are other useful diagnostic aids. Many years ago I was invited to see a 'liver abscess' prior to operation: the patient, an elderly golf caddy, was in fact a case of slow auricular fibrillation with congestive failure due to arteriosclerotic heart disease complicated by a benign tertian malarial relapse. Digitalis and quinine operated upon him instead in a most dramatic manner: digitalis and quinidine, by the way, we sometimes use with much success in selected cardiac cases.

The liver engorgement of advanced congestive failure in mitral disease or in Hanot's hepatic asystole, has in rare instances been regarded as carcinoma of the liver. However, in cancer of the liver, the liver enlargement is not only painful and tender but is also stony hard and irregular: jaundice and ascites are common accidents rather than essential signs: the spleen is very seldom enlarged in the absence of portal thrombosis: a blood-stained pleural effusion may be discoverable: the left supra-clavicular glands may be palpable: cachexia and perhaps pyrexia are present: there may be evidence of a primary growth elsewhere or an operation may have been performed for the removal of a growth within the past five years.

Other causes of painful enlargement are ascending cholangitis, associated with stone, especially in the common bile duct, pyelphlebitis (portal pyæmia) due to septic appendix, suppurating hydatid cyst, and hepatic necrosis.

*Splenomegaly.*—The spleen is the example *par excellence* of a blood depôt. Thus, in acute or recent congestive failure slight splenic enlargement may be detected as a result of

venous engorgement, whereas chronic congestive failure tends to empty the splenic reservoir, thereby leading to splenic atrophy with connective tissue hyperplasia and clinical diminution in the size of the spleen. Cardiac cirrhosis may rarely cause clinically-evident enlargement of the spleen due to portal obstruction, as in ordinary cirrhosis of the liver. Rarely have we been able to palpate the spleen in the circulatory failure of typhoid fever in the absence of enlargement due to other causes. In the absence of malaria, kala-azar, blackwater fever, undulant fever and the tropical splenomegalies, splenic enlargement is an important sign of subacute bacterial endocarditis. Enlargement of the spleen due to acute infections, such as typhoid, typhus, pneumonia, septicæmia or streptococcal fever, subacute bacterial endocarditis, and active rheumatic fever, as a rule being slight and soft, easily escapes detection. In endocarditis lenta (slow but all too sure), however, although the spleen is usually only just palpable, it may become very large from the impact of a constant stream of small emboli on the infected organ. In chronic compression of the heart, enlargement of the spleen is, equally with the attendant ascites, liver enlargement, cyanosis, peripheral œdema, hydrothorax, pulmonary œdema, varicose veins and hæmorrhoids, an expression of the prevailing venous stasis. In blood diseases, the size of the spleen may aid diagnosis: in leukæmia the spleen may seem almost to fill the abdomen: in splenic anæmia, acholuric jaundice and polycythæmia vera the spleen extends perhaps to the level of the iliac crest and to the middle line in front: in pernicious anæmia and in secondary anæmia, splenic enlargement is slight. Polycythæmia hypertonica (Gaisboeck's disease) is either polycythæmia vera with secondary hypertension or of hypertensive heart failure with secondary polycythæmia. Thrombo-phlebitic splenomegaly is commonly diagnosed as Banti's disease. Pulsation of the spleen and aneurysms of the spleen are distinct rarities. Very occasionally a well-marked continuous murmur is heard in splenic enlargements associated with venous engorgement. Splenic friction in acute leukæmia may be slight or gross. We found kala-azar complicated by a left pleuro-pneumonia in a recent case of 'fever with enlarged spleen, splenic friction and liver enlargement'. Palpability and not increased percussion dullness of the spleen is the test of splenic enlargement. The phrenico-colic ligament or rather the shorter gastro-splenic omentum in the adult, it will be remembered, makes the enlarged spleen pass forward and downwards. In children the spleen may enlarge directly downwards. Splenomegaly, especially in the tropics, is of little assistance in the diagnosis of heart disease.

*Ascites.*—Ascites may be defined as a collection of free serous fluid in the peritoneal cavity so that the abdomen becomes converted into a bag of fluid. Its main mechanisms are stasis in

the portal system and inflammation or irritation of the peritoneum. Thus, ascites is either a transudate or an exudate. Indeed the main differential diagnosis of ascites lies between cirrhosis of the liver and chronic peritonitis: they are sometimes found combined in a single case. The causes of ascites in order of frequency are said by Cabot to be, (1) cirrhosis of the liver, (2) heart disease, (3) renal disease (nephritis and nephrotic œdema), and (4) tuberculous peritonitis, especially in children. In the tropics severe anæmias and lymphatic obstruction (filariasis) are important factors. In diseases of the heart, the mechanism of ascites is venous engorgement due to right-heart failure or to failure arising from chronic compression of the heart. The clinical manifestations of chronic compression of the heart are produced by venous stasis and a reduced arterial circulation. Beck has assembled a diagnostic triad which the practitioner may find helpful in the diagnosis of chronic compression of the heart. It consists of—(1) ascites and liver engorgement, (2) high venous pressure, and (3) a *small quiet heart*. In this syndrome the cervical veins stand out like goose quills and pulsus paradoxus is frequently present. Not unreasonably, Beck regards as a confusing mass of medical verbiage such terms as adhesive pericarditis, concretis pericardii, symphysis cardiaca, pericarditic pseudo-cirrhosis of the liver, mediastino-pericarditis, Pick's disease, Concato's disease, and polyserositis. The compressing agent in chronic compression of the heart may be fluid (sterile or infected), scar tissue, neoplasm, or a combination of several of these lesions. [In acute compression of the heart, as for example when a myocardial infarct or contusion ruptures, the liver has not had time to enlarge. Its diagnostic triad however is (1) low arterial pressure, (2) high venous pressure, and (3) a small quiet heart.] In protracted right-heart failure of rheumatic, arteriosclerotic or rarely syphilitic origin, recurrent ascites may figure so prominently that chronic compression is simulated. The term hepatic heart failure or asystole hepatique was used by Hanot to describe a series of congestive failures characterized by considerable liver engorgement over months or years, with recurrent ascites and without notable deterioration in the general health notwithstanding these morbid phenomena. Clinical cardiac cirrhosis is rare: its diagnostic criteria are preponderant ascites, a small liver, supernormal venous pressure and a palpable spleen. 'The sudden onset of ascites or of hæmatemesis and their recurrence, accompanied by considerable splenic enlargement, might suggest the presence of portal thrombosis'.—Rolleston. Cirrhosis of the liver, however, would be a safer diagnosis. Horder has stated that ascites arising insidiously in a woman in whom there are no other symptoms or signs for example of heart, kidney or liver disease, is generally due to ovarian adenoma.

The clinical signs of ascites are shifting dullness, fluid thrill and signs of portal-peripheral anastomosis. When testing for shifting dullness, the examiner should wait a few moments after the patient has rolled over on to his side, to permit the fluid to seep through the mesenteric and intestinal folds: it does not run over the sharply projecting spinal column as over a waterfall. Tympanites is especially common in heart failure. It commonly masks ascites. Its presence in high degree should lead to a more careful search for free fluid in the peritoneal cavity.

The tempo of accumulation of cardiac ascites is the most rapid of all forms of ascites, just as that of tuberculous ascites is usually the slowest. If the quantity of ascitic fluid is large and its accumulation has been rapid, the abdomen is more or less globular, the umbilical region is prominent and there is a tight sensation of the belly, sometimes amounting to actual pain, due to the stretching of the abdominal wall. If the quantity of ascitic fluid is large and its accumulation has been gradual, then bulging of the flanks is more prominent, the lower ribs are pushed outwards and upwards and the epigastric angle is widened. Hæmorrhagic ascitic fluid usually means cancer. The chemical characters however of ascitic fluid are of little help in the differential diagnosis of ascites. Never omit to make a rectal examination for small collections of fluid and secondary deposits from gastric cancer in the recto-vesical peritoneum and a vaginal examination. The knee-elbow position, for the detection of small collections of fluid, is a gymnastic exercise ill-borne by cardiacs: it should be omitted.

*Cardiac hydrothorax*.—Hydrothorax is defined as a collection of clear fluid in the pleural cavity, the result of passive transudation from the capillaries. The essential mechanism of cardiac hydrothorax is engorgement of the pleural venous system (the pleural sacs have both a systemic and a pulmonary venous drainage, i.e., the superior vena cava and the pulmonary veins) with resultant increased hydrostatic pressure in the capillaries—capillary hypertension. A further factor is the lowered colloid osmotic pressure of the plasma by reason of the relative permeability to protein of the capillaries of the serous cavities. Hence in heart failure, osmotic factors associated with increased capillary permeability co-operate with capillary hypertension in the production of effusions into serous cavities as potently as does the mechanical factor of gravity in the production of œdema of the ankles and lower limbs. The combination of pulmonary and systemic congestion, i.e., of left- and right-heart failure, is most favourable to the development of cardiac hydrothorax, whereas systemic venous engorgement alone determines the occurrence of peripheral œdema. Evan Bedford has found that left ventricular stress and failure with regular rhythm favours the development of left hydrothorax and that

left ventricular failure with auricular fibrillation predisposes to right hydrothorax. The classical domain, however, of hydrothorax is right-heart failure. The theories advanced to explain the right-sided predominance of cardiac hydrothorax are at least sufficiently numerous. We have tapped a right-sided cardiac hydrothorax twelve times: this patient now has considerable ascites as well but no radiological evidence as yet of fluid in his left pleural cavity.

Although hydrothorax may herald the other signs of failure in the systemic circulation, it is more commonly masked by the gross manifestations of congestive failure. The physician should, however, make a deliberate clinical and radiological search for evidence of hydrothorax supervening in any case of congestive failure that suddenly manifests distressing oppressive dyspnoea, more evident cyanosis and a general accentuation of the signs of right-heart failure. Such a sudden worsening of the clinical status in congestive failure may be ascribed in the main to the reduced vital capacity, the interference with the pulmonary ventilation and the increased intrapleural pressure attendant upon the sudden development of cardiac hydrothorax. Further, elevation of the venous pressure is caused by the increased intrapleural pressure. The cardinal signs of hydrothorax are those of a pleural effusion—namely, (1) percussion dullness, (2) displacement of the heart, (3) annulled vocal fremitus, (4) diminished and altered or absent breath sounds—*minus* friction sounds and fever.

As transudations take place into the pleural cavity, absolute and toneless percussion dullness may be detected at the extreme base, together with a correspondingly increased sense of resistance. The dullness gradually extends upwards and slight variation of the dullness with the position of the patient may be demonstrable. The prevailing intrapleural pressure is negative, more so on the right side than on the left. Immediately fluid accumulates in the pleural cavity the lung on that side collapses. The elastic traction exerted on the mediastinum by the lung on the affected side is thus removed, leaving unopposed the traction of the sound lung with consequent mediastinal shift to the opposite side. The contents of the middle mediastinum, it will be remembered, are almost totally the heart and its coverings. Hence, when fluid is poured out into a pleural cavity, the heart is invariably and instantly displaced to the opposite side, in the absence of fixation of the heart by adhesions and of consolidation or of fluid at the opposite base: approximately one case of hydrothorax in three is bilateral. Enlargement of the heart and the possibility of an associated hydropericardium must be borne in mind in the assessment of cardiac displacement. In the latter case, the apex beat (*i.e.*, the point on the surface of the chest, furthest downwards and outwards, at which the impulse can be distinctly felt) is generally pushed upwards and to the

left, and lies, when it is palpable at all, distinctly within the left border of cardiac dullness and not, as in cardiac enlargement, in close relationship with it. Absence of vocal fremitus ranks third in importance and is due to the interposition of fluid which is a poor conductor of the laryngeal vibrations to the chest wall. Routine auscultation in congestive failure commonly reveals persistent moist sounds at the bases. Diminished breath sounds and diminution of the whispered voice sound at a base in congestive failure should suggest basal collapse and attendant bronchitis consequent upon hydrothorax. A collection of 500 c.cm. or over will yield the signs described. We must not forget that hæmorrhagic infarction of the lung is a common and often repeated complication of advanced congestive failure and that it more commonly involves the lower and middle lobes of the right lung, because the right pulmonary artery affords a wider entrance for pleural emboli from the right heart and from the deep pelvic veins which latter may suffer thrombosis in cases long confined to bed.

The removal even of 500 c.cm. in cardiac hydrothorax gives the patient remarkable relief and facilitates the action of digitalis and salyrgan, much as a timely venesection may do. The character of the transudate may approximate that of an exudate.

As Evan Bedford has remarked on his paper on left ventricular failure (1939) radiological study will occasionally reveal an interlobar or encapsulated hydrothorax (hydrothorax saccatus interlobaris) due to transudation from the visceral pleura consequent upon pulmonary congestion.

*Oliguria.*—Oliguria, remarks Fishberg, is a cardinal manifestation of systemic venous stasis. In our wards the urinary output curve is shown on the temperature chart of the heart case. It depicts the progress of right-heart failure. If a patient with right-heart failure states that his urine is abundant this should excite a suspicion of complicating diabetes mellitus. Horder states, 'Both chronic nephritis and dilatation of the heart may lead to a scanty, albuminous urine. But in the case of chronic nephritis the scanty urine is usually pale, pigment elimination being diminished, is free from or has but a small deposit, the amount of albumin is always considerable, and renal casts are present. Whereas in dilatation of the heart the scanty urine is high-coloured, contains a large uratic deposit, the amount of albumin is very variable, and renal casts are absent'. Unfortunately, many heart cases are renal cases as well. In acute heart failure, *e.g.*, in coronary thrombosis, oliguria bespeaks systemic hypotension and may proceed to anuria.

#### Remarks

The manifestations of increased venous pressure dominate the clinical picture of right-heart

failure, which in its pure form is not accompanied by pulmonary congestion. Dyspnoea may be caused by associated hydrothorax, ascites, and severe liver engorgement. Dyspnoea, however, is an almost invariable symptom in right-sided failure because, as we have stated elsewhere (Kelly, 1939), its causes, e.g., left-heart failure, etc., essentially implicate the pulmonary circuit. Armstrong has recently described a case of heart failure restricted to the right ventricle. Evan Bedford and Harrison hold the view that unilateral hypertrophy, dilatation and failure not only may occur but usually do occur. Venesection has no place in the treatment of primary right-heart failure, or of acute right ventricular failure due to pulmonary embolism. Congestive failure is associated with cardiac enlargement except in chronic compression of the heart. The presence of marked chronic passive congestion of the liver, lungs and other viscera and of extensive myocardial lesions often render it quite unnecessary to invoke toxæmia or exhaustion to explain the advent of heart failure in subacute bacterial endocarditis.

#### *Jaundice in heart disease*

In clinical heart disease jaundice may be either latent or frank. We have already referred to latent jaundice in second and subsequent attacks of right-heart failure. Latent jaundice is evidenced by a subicteric tint of the conjunctiva and skin, or is altogether masked by attendant cyanosis. The cause of latent jaundice here, as in subacute bacterial endocarditis, is increased blood destruction, due in the first case to prolonged anoxæmia and to *Strepto. viridans* in the second case. Frank jaundice is not common in heart disease. It suggests three possibilities, that (1) severe right-heart failure has superimposed congestion upon an already damaged liver, that (2) the case is one of severe and long-standing right-heart failure due to marked mitral or tricuspid stenosis, or that (3) pulmonary infarction is now complicating congestive failure. The latter complication is suggested by an abrupt worsening of the clinical status of the patient: there is a sudden increase in heart failure and cyanosis with a sudden onset of jaundice or a sudden accentuation of any existing jaundice, or jaundice appears two or three days after the lung infarction. The coloration of frank jaundice in heart disease is less deep than that of obstructive jaundice. Cyanotic icterus connotes yellowing of the conjunctiva and facial skin *plus* cyanosis of the lips and ears: this facies is of grave import. The unusual distribution of jaundice in congestive failure was first indicated by Meakins who reported that in a case of congestive failure he observed that the œdematous lower part of the body was free from jaundice whereas the upper part was markedly jaundiced and free from œdema. This observation holds also of course for cyanotic icterus. Page later reported two

cases of congestive heart failure with hemiplegia wherein the paralysed side was œdematous, and the sound side was icteric. Ottenburg (1932) explains this strange phenomenon by the low solubility of bilirubin which is held in the blood adsorbed to protein because of the lower protein content of the œdema fluid. According to Ottenburg two or more of the following factors are responsible for the production of jaundice in congestive failure—

- (1) Increased production of bilirubin especially in the lungs, spleen and liver due to the destruction of red cells, as a result of the slowed circulation and prolonged anoxæmia.
- (2) Profound depression of the excretory function of the intact liver cells for bilirubin as the direct result of lack of oxygen.
- (3) Actual atrophy of the liver cells at the centres of the lobules as a secondary result of anoxæmia.
- (4) Slowing of the circulation so that only a small fraction of the usual amount of blood passes through the liver to be cleared of its bilirubin.

Two special points emerge from the fact that anoxæmia constitutes the essential mechanism of cardiac jaundice.

(1) Failure not only of the right heart but also of the left heart seems to afford the most favourable circumstances for its production.

(2) Cardiac jaundice is a clear indication for oxygen therapy.

#### ACUTE HEART FAILURE

In general, the clinical picture of ordinary backward or congestive failure is dominated by upstream manifestations, i.e., by congestion behind the failing left and/or right chambers, rather than by inadequate output of the failing chamber. Acute heart failure is compounded of peripheral circulatory failure (shock) and of congestive cardiac failure; for example, in coronary infarction the sudden injury to the heart not only disables the cardiac pump but also initiates peripheral circulatory failure of hæmatogenic type (secondary shock). In general, the clinical picture of acute heart failure is dominated by downstream manifestations, i.e., by forward failure or by signs of acute circulatory collapse due to an inadequate blood supply to the tissues. Thus, in acute heart failure, whilst the downstream features of peripheral circulatory failure declare themselves, the upstream symptoms and signs of congestive right- and left-heart failure have to be looked for. Hence, when the practitioner is confronted with a case of acute circulatory collapse his first consideration must be as to whether he is dealing with a fundamental defect in the central cardiac pump (acute heart failure) or with a fault confined to the peripheral vascular apparatus (peripheral circulatory failure). His decision will hinge on the presence or absence of upstream manifestations. If there are no symptoms or signs of left- or right-sided congestive heart failure there can be no sort of heart failure. Hence acute heart failure will display evidence of left-heart failure, such as dyspnoea, orthopnoea, and pulmonary congestive

signs and signs of right-heart failure, such as engorged cervical veins and liver engorgement. Collapsed cervical veins, on the other hand, speak a very low venous pressure significant of peripheral circulatory failure. Fishberg's implication that cases of coronary thrombosis are divisible into those with shock and those with heart failure does not constantly accord with our experience. We are of opinion that signs of heart failure appear coincidentally with shock in coronary thrombosis about as frequently as they fail to appear in coronary thrombosis without shock. The diagnosis of coronary thrombosis is further advanced by the discovery in the heart itself of signs suggestive of cardiac damage, such as heart sound failure, gallop rhythm, and cardiac arrhythmias. Tic-tac rhythm is more characteristic of peripheral circulatory failure than it is of organic heart disease: even when it does occur in organic heart disease the circulatory state is usually that of acute heart failure. Cardiac enlargement and murmurs usually have antedated infarction. The final proof of myocardial damage, *i.e.*, of infarction, is as a rule to be found in the coronary thrombotic pattern of the electrocardiogram.

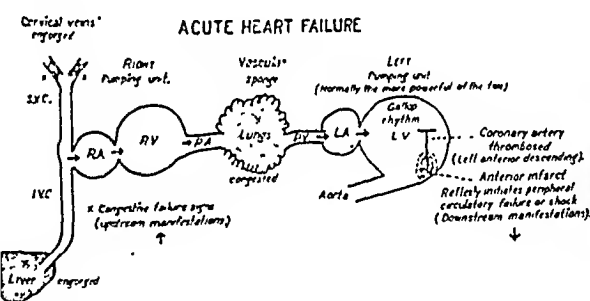


Diagram illustrating cardiac collapse in coronary thrombosis.

The clinical picture of coronary thrombosis may be summarized as follows:—

- (1) Pain due to coronary insufficiency setting in acutely and producing a relative localized myocardial ischaemia and anoxaemia which not only outlasts 20 minutes but goes unrelieved by any existing collateral inter-coronary anastomotic circulation.
- (2) Peripheral circulatory failure (downstream manifestations).
- (3) Congestive failure (upstream manifestations).
- (4) Clinical evidence of myocardial necrosis such as fever, sweating, leucocytosis or increased sedimentation rate.
- (5) Persistent electrocardiographic changes.
- (6) The appearance of acute pericarditis as revealed by a friction rub.
- (7) The occurrence of embolism, especially in septal infarction.

Libman holds that hyposensitive individuals are more apt to exhibit coronary thrombosis in terms of shock rather than of pain. Their relative inability to feel pain may puzzle the diagnostician, not only in cases of coronary thrombosis but also in other conditions, such as

duodenal ulcer. Painless coronary thrombosis, however, is commoner in those displaying some degree of congestive failure. In these latter subjects pain equivalents or substitution symptoms, usually a seizure of dyspnoea, proclaims the onset of coronary thrombosis.

Rapidly developing injury to the myocardium, productive of cardiac collapse, is likewise responsible for the induction of acute heart failure in some cases of diphtheria. We have already referred to the acute heart failure induced by paroxysmal tachycardia: other tachycardial arrhythmias such as flutter and fibrillation may similarly precipitate acute heart failure. A third group of acute heart failures is due to sudden and pronounced mechanical hindrance to the heart in carrying out its work, *e.g.*, to cardiac tamponade (sudden accumulation of blood or fluid in the pericardium), massive pulmonary embolism, ball-valve thrombus obstructing the mitral orifice.

The Adams-Stokes' syndrome is the classical example of acute heart failure of syncopal type. Some cases are due to transient attacks of ventricular fibrillation and not to lesions of the conduction system; asystole results in either circumstance. The main disturbance is obviously an inadequate blood supply to the brain or rather a paroxysm of cerebral ischaemia, productive of a seizure of unconsciousness. Heart failure in cardiac syncope or the syncopal type of acute heart failure is almost instantaneous and consciousness is lost because the diminution of the cardiac output is sudden and severe. The clinical picture here resembles that of the neurogenic type of peripheral circulatory failure (primary shock), such as a pugilist may display on the receipt of a blow on the solar plexus. The characteristics of the Stokes-Adams' syndrome are bradycardia, syncope, and convulsions, even in recumbency. In the gravest attacks the patient lies unconscious and motionless. The facies, especially of the previously ruddy-faced individual, is most striking: he now presents an ashen-grey or livid corpse-like aspect with glassy dull eyes, widely dilated pupils and sometimes conjugate deviation. The cervical veins are enormously engorged. There is a gasping respiration every 30 seconds. Respiration may, however, be stertorous and suggestive of cerebral haemorrhage or Cheyne-Stokes' breathing may develop. No pulse is felt and no heart sound is heard for 2 to 3 minutes. The sphincters are relaxed and Babinski's sign may be elicited. Then the face flushes pink and the pulse returns and the heart sounds are heard. The breathing is resumed within 1 to 2 seconds and consciousness returns within a few seconds. The patient is dazed for 15 to 30 minutes. The attack is ended.

In the cardiac collapse (coronary thrombosis) type of acute heart failure, heart failure sets in less acutely than in this cardiac syncopal type of acute heart failure. Loss of consciousness too is unusual in the former type, although we



do see occasional cases of coronary thrombosis ushered in with loss of consciousness.

*Blood pressure recordings.*—The fall in blood pressure which attends the onset of coronary thrombosis has long been regarded as one of the most striking manifestations of the altered hæmodynamics of this condition. Nevertheless, in 1937 we found to our surprise that certain physicians delicately refrained from taking the blood pressure in suspected or actual coronary thrombosis. They had been unduly alarmed by the 'dangers of blood pressure examinations in coronary thrombosis' (Hyman and Parsonett, 1932). These dramatic writers alleged that the attending physician's blood pressure recordings 'undoubtedly played a sinister part' in the untimely death of an old lady of 70, who developed peripheral embolic blockage after coronary thrombosis. As I read this indictment of the unfortunate general practitioner in the case, I felt that he might well have derived a modicum of comfort from Pascal's observation: 'The doctor sometimes cures, sometimes kills, *but he always consoles*'. Whilst we deprecated frequent fussy baumanometric measurements, we nevertheless continued our rapid routine reading of the blood pressure in this emergency without any suggestion of a mishap. And so the local trepidation associated with the recording of blood pressure in coronary thrombosis quickly subsided.

Sometimes in the painful stage of coronary thrombosis, peripheral vaso-constriction associated with the attendant shock, causes an early rise to precede the fall in blood pressure which ordinarily documents coronary thrombosis. An attack of angina pectoris is often accompanied by a rise in the blood pressure but the time-test and other features generally prevent confusion. Peripheral vaso-constriction may likewise sustain or even further elevate the blood pressure in hypertensive heart failure. Indeed in 'high pressure stasis', the blood pressure may fall only when the heart, the powerhouse of the circulation, is repaired somewhat by rest, digitalis, and diuretics. In fact, if the blood pressure does not now decline, this indicates that the insufficient hypertensive heart is not responding satisfactorily to treatment. In 'low-pressure' failures, on the other hand, a rising blood pressure commonly signifies an improving heart muscle.

#### HEART SOUND CHANGES IN ACUTE AND IN ORDINARY HEART FAILURE

We shall again take coronary thrombosis as our example of acute heart failure. In *Diseases of the Coronary Arteries and Cardiac Pain*, by Levy, Paul White and others, it is briefly stated that in coronary thrombosis 'the heart sounds are weak and tic-tac or gallop rhythm may be heard'. In *Diseases of the Heart* by Lewis it is still more briefly stated that 'The heart sounds (in coronary thrombosis) are indistinct, gallop rhythm is frequent'. Some expansion of these

remarks concerning the heart sound changes in coronary thrombosis may enhance their diagnostic value for the general practitioner.

If the first heart sound is suddenly observed to have become faint and muffled and the second relatively loud in an individual previously known to possess a normal intensity of his first and second heart sounds, then these altered heart sound findings are highly significant of a sudden impairment of the contractility of the heart, i.e., of an acute heart failure, such as coronary thrombosis. Heart sound recordings in coronary thrombosis indicate that the muffling of the first sound is caused by a loss of high frequency vibrations due to either a loss of muscle tone or change in intraventricular pressure, the result of the injury to the heart muscle. However it may be, this faintness and muffling of the first heart sound in coronary thrombosis is best appreciated at the apex where the ventricle abuts on the chest wall. In one's appreciation of the coincident relative loudness of the second heart sound at or to the left of the apex, especially in elderly subjects with possible aortic sclerosis, it is well to recall that the second sound heard in the aforementioned area is mainly the transmitted aortic component of the second heart sound. In all affections of the myocardium the physician should note also the loudness of the first sound at the base, where normally the first heart sound is rather less loud than the second sound. In coronary thrombosis the heart sound alterations observable at the apex are likewise detectable at the base where however the first sound disappears long before it does at the apex. Systemic hypotension weakens the aortic second sound. In the acute heart failure of coronary thrombosis described here the heart sounds at the base are usually inaudible. The obesity of many men and women in Bengal is commonly so gross as to render satisfactory auscultation, even of the relatively normal heart, impossible except for those endowed with really good hearing. In these obese subjects the heart sounds are not infrequently best heard over the xiphisternum, where however one or both sounds may have a peculiar scratch or grunch which must not be confused with pericardial friction. Likewise in emphysema the heart sounds are often best heard over the epigastric angle, where however they may take on a ringing metallic quality from the flatulent stomach so common in these subjects. A special failure of the first sound at the apex as contrasted with that at the xiphoid cartilage together with coincident weakness of the aortic second sound has been reported in some cases of coronary thrombosis. Sometimes in coronary thrombosis the almost complete muffling of the heart sounds everywhere resembles the 'silent heart' one associates with a large pericardial effusion. Overacting heart sounds, on the other hand, occasionally attend coronary thrombosis: in severe cases they herald a further thrombosis or congestive failure: in less severe cases they



become progressively less demonstrative. Some cases of coronary thrombosis show no detectable heart-sound changes.

Whereas feeble heart sounds are almost the rule in acute heart failure, loud heart sounds may sometimes be heard in chronic or ordinary congestive failure. Most writers have stressed the fact that in the stage of failure, mitral stenosis retains its snappy first sound even when the characteristic murmur has altogether disappeared and that the sounds of the thyrotoxic heart tend to retain their loud and angry character. Few, however, have commented upon the fact that in some cases of congestive failure the sounds become louder with the development of failure and then become fainter when failure recedes or when final circulatory collapse supervenes. The practitioner is naturally nonplussed by these loud heart sound findings in congestive failure because tradition has led him to expect heart sound failure coincidently with heart failure. I have been interested for many years not only in loud heart sounds in certain congestive failures but also in loud gallop rhythm, the extra sound of which is sometimes far from being the soft thud that the tradition-bound might anticipate.

#### ANGINA PECTORIS

'In this secret and fell disease', remarked Clifford Allbutt, 'there is a fascination to which no physician is a stranger, a fascination in its dramatic events and in the riddle to read'.

'The only established mechanism of cardiac pain', concludes Fishberg, 'is ischaemia of the myocardium—others are purely hypothetical'. In our view, the theory that does not bear the test of practice should be revised or rejected. Thus, Allbutt's aortic theory is at once put out of court by its signal failure to explain the likelihood of sudden death in angina pectoris. This most unpleasant possibility follows angina pectoris like its shadow. In the opinion of Keefner and Resnik, the likelihood of sudden death is indissolubly linked with the underlying mechanism of angina pectoris. In consonance with our conception of the mechanism of angina pectoris the cause of sudden death in this condition is ventricular fibrillation due to sudden myocardial anoxaemia.

Angina pectoris is a chronic recurrent symptom-complex due to paroxysms of localized relative myocardial ischaemia, the result of coronary insufficiency of less than '20 minutes' in duration (usually less than 3 minutes by the clock). It may occur on exertion, on emotion, during rest, or during sleep. Repeated attacks induce replacement fibrosis in myocardial localities afflicted by coronary arteriosclerosis and constantly under-nourished in consequence thereof. Myocardial weakness and congestive failure are the logical sequelae of such a progressive replacement of myocardial fibres by connective tissue. Angina pectoris, however, inhibits activity. Hence, as a rule, congestive

failure does not supervene until after coronary thrombosis has complicated the course of angina pectoris. Indeed, angina pectoris may now altogether disappear as a result of local necrosis of the P-factor producing area. Perhaps more commonly congestive failure and auricular fibrillation limit activity and thus obviate attacks of angina pectoris. On the other hand, the higher oxygen requirements of the dilated heart and the lowered coronary income in failure lead to more frequent seizures of angina pectoris. In the last-mentioned circumstances, the physician should exhibit digitalis (tablets digitalis folia, gr. 1, *b.d.*, *p.c.*, or  $\mathcal{R}$  tincture digitalis, m. x, aquam chloroformi, ad.  $\mathfrak{z}$  1, *t.d.s.*, *p.c.*) and not nitrites, for the relief of anginal pain. Digitalis is probably harmful in angina pectoris associated with a small or normal-sized heart.

Certain remarks made years ago by Parkinson and Bedford are much in vogue to-day. Concerning angina pectoris they used to say that 'an individual either has angina pectoris or he has not'. They severely disapproved of 'anginoid pain' and of such misleading and apologetic terms as 'mild angina', 'secondary angina' and 'pseudo-angina' or 'false angina'. They heartily endorsed Potain's dictum that 'there are no false diseases: there are only false diagnoses'. Whenever possible a diagnosis of angina pectoris should include a statement of its aetiology, *e.g.*, coronary arteriosclerosis, hypertensive arteriosclerotic heart disease, aortic insufficiency, syphilitic aortitis with ostial stenosis, calcific aortic stenosis, paroxysmal tachycardia, coronary embolism, arterio-venous fistula, thrombo-angiitis obliterans, periarteritis nodosa and mycotic aneurysms of the coronary vessels, and so forth.

Coronary arteriosclerosis and cardiac hypertrophy usually combine in varying dominance to narrow the coronary reserve. Thus, angina pectoris in the middle-aged and elderly is commonly due to the summation of hypertension and coronary arteriosclerosis: the grade of the latter is usually insufficient in itself to yield angina. Indeed, angina pectoris may be the main complaint of a hypertensive arteriosclerotic heart disease subject until congestive failure or coronary thrombosis supervenes. In the renal hypertension of young persons and of eclamptics, on the other hand, angina pectoris is distinctly rare because coronary arteriosclerosis is absent herein. Hypertensives of both sexes and especially menopausal hypertensive, like rheumatic heart disease sufferers, are remarkably prone to develop cardiac neuroses. It should, however, be borne in mind that cardiac neurosis or neuro-circulatory asthenia may overlie and obscure the presence of angina pectoris in the hypertensive arteriosclerotic heart disease subject: evidence of vascular vulnerability elsewhere, *e.g.*, absence of pulsation of the dorsalis pedis arteries, intermittent claudication, retinal arteriosclerosis, peripheral arteriosclerosis, etc., would favour the presence of a complicating angina pectoris in

such case. A doctor of the last century observed with more cynicism than accuracy that 'the man with arteriosclerosis of his radial arteries has warmed both hands before the fire of life'. Coronary thrombosis is a much more likely accident in coronary arteriosclerosis without hypertension than in hypertensive arteriosclerotic heart disease. Hence the prognosis of the latter is correspondingly more cheerful. The incidence of angina pectoris and of coronary failure in Indians is engaging our attention at the present time. Coronary failure, by the way, is attended by pain and shock as in coronary thrombosis, but is found wanting in respect of permanent electrocardiographic changes and of the evidences of heart muscle necrosis. So far, we have been impressed by the great rarity of angina pectoris in Indians notwithstanding their relatively high incidence of hypertensive arteriosclerotic heart disease and of coronary thrombosis. Incidentally, some writers inaccurately employ the term chronic myocarditis to describe the clinical picture associated with coronary artery disease. Pathologically chronic myocarditis is a chronic but active inflammatory lesion of the myocardium due to bacterial or non-bacterial excitants. As the damage associated with disease of the coronary vessels is due to nutritional changes, the term arteriosclerotic heart disease states what we know and not what we imagine. Angina pectoris is associated with narrowing of one or more of the larger coronary vessels. The senile heart is characterized by extensive or diffuse arteriosclerosis of the finer coronary branches.

'Angina pectoris', states White, 'is a symptom of individuals in the upper walks of life'. We do not subscribe to this notion that angina pectoris is largely a matter of tone, social atmosphere, or something a plain medical writer cannot convey. Just as a history of lightning pains justifies the diagnosis of tabes dorsalis on the history alone, so does a history of effort angina justify the diagnosis of angina pectoris solely in its symptomatology. In general, the pain of angina consists of combinations in varying preponderance of two pain components: it consists of pain transmitted directly and indirectly from the heart. It is notoriously susceptible of misinterpretation by the patient. Its character and distribution may be quite atypical. If, for example, the discomfort begins in the epigastrium after meals, is associated with belching, and is apparently relieved by alkalis, the patient will naturally insist that it is 'indigestion'. In fact, angina pectoris quite frequently does masquerade under the guise of indigestion. If angina pectoris is coincident with some non-cardiac disease, the anginal distress may become hopelessly commingled with and entangled in the symptomatology of the concomitant non-cardiac disorder. Thus, not infrequently the definition and differential diagnosis of angina pectoris may occasion even an experienced physician quite considerable

difficulty. In our experience less intelligent patients are often hopelessly incapable of detailing the more complex forms of anginal pain: when called upon to do so they usually grin in an apologetic and speechless manner, utter a few fragmentary human noises and depart with a McLean's powder for their 'indigestion'. Their educational level and discriminating and descriptive powers are totally inadequate for the crucial portrayal of the pain, upon which the diagnosis of angina pectoris is fundamentally based. Little wonder that statistics show that the highest incidence of angina pectoris is amongst the medical profession and the lowest amongst the day-labourer and the farmer. The other factors responsible for this divergent class incidence shall be discussed later.

Libman, Fishberg, White and others have fittingly stressed atypical forms of angina pectoris and the practitioner would do well to bear these forms in mind, especially when dealing with middle-aged patients, labelled 'arthritis of the left shoulder' or 'neuritis of the arms'.

Atypical angina may be encountered in the form of a persistent dull aching pain, in the left more often than in the right shoulder region. The pain is unaffected by exercise or nitrites: it is irresponsive to physical therapy, the form of treatment generally sought by the patient: it is often worse at night and morphine may be required to secure sleep. This shoulder pain is not the usual radiation of the sub-sternal pain to the left shoulder and left arm. It is a continuous and intractable pain that, in our experience as in that of others, may precede or follow angina pectoris or cardiac infarction. We have not found any local radiological changes in these shoulder pain cases. A sub-deltoid bursitis was found in one case by my surgical colleague. But the precise mechanism of this shoulder pain remains obscure.

Spillane and White have recently reviewed a group of patients with eccentrically placed anginal pain, the mechanism of which is likewise obscure. 'A long-recognized example of these larval or fractional forms of angina pectoris', they stated, 'is that in which pain on effort appears only in the arms, the crucial sub-sternal pain being absent'. This eccentric pain of angina pectoris has been described by Herbeden, Osler, Allbutt, and Mackenzie. Retrograde angina or Potain's *angina reuversee* is another eccentric and interesting form of angina pectoris. 'The flow of pain is reversed: it starts in the wrist, elbows or jaw and only settles behind the sternum when fully developed, so that on exertion a patient may complain of pain in the wrist or teeth'—Evan Bedford. In our view, Vaquez's retrograde angina arising in the rectum is a visceral hysteria and in support of this opinion certain remarks of Clifford Allbutt are worth quoting in their entirety: 'What, I repeat, should we think of a lecturer who threw together into the same class and under the same name the functional hemiplegias of

hysteria and the hemiplegias due to cerebral disease. Surely it is levity to confuse the sequels of unstable "neurotics", mostly women, with the assault of one of the fiercest and most searching afflictions which can fall upon steadfast and resolute men. But the most egregious example of this eccentricity which I have noted is the description, by a well-known modern physician, of a case of "angina pectoris originating in the clitoris"!

Conversely in gall-bladder disease, pain arising in the gall-bladder may radiate down cardiac pathways sensitized by coronary artery disease.

The up-to-date practitioner readily recognizes the distinctive features of neurocirculatory asthenia, including left mammary pain. In consequence there has been a notable and gratifying decline in the erstwhile popularity of 'angina pectoris'. When, as Harrison has pointed out, angina pectoris, præcordial aching due to the heart consciousness of cardiac neurosis and reflex soreness of the pectoral muscles are present in the same patient there is considerable danger, unless a careful history is taken, that the significant pain may be masked by the two unimportant sensations. Such a case is very briefly presented at the end of this note.

There is an interesting group of cardiac neurotics, exclusively women, of considerable therapeutic importance in that they respond poorly and react badly to the barbituric acid group of hypnotics and sometimes to morphine as well. Alvarez, who first identified these peculiar women in his abdominal practice, well describes them as hypertensive, overactive, markedly fatigued and somewhat psychopathic. Our own impression is that these women 'fight' the barbiturates. In spite of, say, ten grains of medinal at bedtime, patients with this idiosyncrasy truthfully report next morning that they 'hadn't a wink of sleep', or that they had 'snatches of sleep with terrible nightmares'. Chloral is about the only drug that induces satisfactory sleep in these nervy women:  $\mathcal{R}$  Syrupi chloral and tincturæ valerianæ ammoniatæ, of each 3ss, ammonii bromide, grs. x, aquam chloroformi ad. 5i. Sig. 5i secundis horis, ad. doses IV. S.O.S. Passiflorine is their best general sedative: one teaspoonful in glucose water after the midday and evening meal for 20 days.

A classical example of this temperament and idiosyncrasy was lately under our care.

Anglo-Indian lady with 'a long history of nervous heart attacks'. Six weeks prior to admission she had a very bad 'attack' with vomiting which even morphine failed to control: in fact she felt worse after morphine. Medinal and luminal had, she said, 'given her insomnia and left her a bundle of nerves'. Our diagnosis was coronary thrombosis type III six weeks ago; angina pectoris supervened; cardiac neurosis localized to præcordium (to the organ inferiority of Adler and somatic compliance of Freud); reflex soreness of the left pectoral muscles; idiosyncrasy to barbiturates; no discoverable septic foci (septic teeth, tonsils, etc., may underlie cardiac neurosis).

#### ELECTROCARDIOGRAPHIC INTERPRETATIONS

Thomas Lewis stands at the origin of electrocardiographic interpretation. He stated in the most lucid and conclusive fashion the fundamental principles of clinical electrocardiography. He thought out and made of one piece, solid and permanent the whole system of electrocardiography. As this man of genius has remarked (1937), 'electrocardiography has taken us far, having filled great gaps in our knowledge of these maladies (heart disease), for it is a means of directly examining the all-essential heart muscle'. Unfortunately, however, states Master (1939) 'there has been neglect of the fact that identical changes in the electrocardiogram may result from alterations in the size, shape, and position of the heart, in the absence of any myocardial disease whatever'.

Changes in the electrocardiogram may be due to—

- (1) Cardiac arrhythmias,
- (2) Muscle damage, acute or chronic,
- (3) Alterations in the size, shape, and position of the heart,
- (4) The action of certain drugs, notably digitalis, quinidine, and morphine.

An impression lying down at the bottom of my mind for a long time is that many physicians do not appreciate the dependence of the cardiogram upon (3) which include such factors as age, body position, habitus, obesity, pregnancy, hypertension, valvular disease, congenital heart disease, pulmonary disease, and chest deformities, which alter the contour of the heart. Thus, certain electrocardiographic changes are being constantly mis-interpreted as evidence of myocardial damage, as in fact 'toxic myocarditis', 'rheumatic infection' or 'coronary sclerosis', when in reality myocardial disease is altogether absent and the electrocardiographic changes in question merely reflect some alteration in the size, shape, or position of the heart.

An up-country primipara, aged 22 years, in the last trimester of pregnancy was recently referred to me for opinion as to her heart. Her previous history was excellent. Lately, she had become aware of exertional palpitation. Her local doctor discovered 'extra-systoles' and hastily, albeit most carefully, transferred her to an electrocardiographer in Calcutta. Her cardiogram showed left axis deviation, a large  $Q_3$ , and an inverted  $T_3$ , which, being interpreted, spelled 'coronary sclerosis and toxic myocarditis'. The general condition of the patient was excellent. Radiography confirmed a raised diaphragm with a transverse lie of the heart which was not appreciably enlarged. Her investigation was otherwise negative. Her tracing was regarded as a pregnancy effect, due to the transverse position of her heart. A diagnosis of gestatory heart disease (functional heart disease of pregnancy) was made and no special restrictions were imposed. The lady's pregnancy and puerperium were quite uneventful.

Gestatory heart disease is a physiological syndrome produced by one or more of the following factors: increased cardiac work as the result of the increased demands of pregnancy, changes in the position of the heart, the arterio-venous fistula-like action of the placenta. Circulatory function commences to return to normal even before delivery. The circulatory peculiarities of the acute phase of beri-beri also bear a striking resemblance to those of arterio-venous aneurysm. Classical examples of 'reversible heart' are encountered in myxœdema, beri-beri, arterio-venous aneurysm, and congenital cavernous hæmangioma.

In neurocirculatory asthenia, rotation of the perfectly healthy though long, narrow, vertical or hanging-drop type heart, produces right axis deviation, large P-waves, low QRS<sub>1</sub>, high QRS<sub>2</sub>, and QRS<sub>3</sub> and even inversion of T<sub>2</sub> and T<sub>3</sub>. Hence the subject of neurocirculatory asthenia who escapes an electrocardiographic misdiagnosis of either 'rheumatic infection' or 'toxic myocarditis' is indeed twice blessed.

We freely acknowledge the fact that acute tonsillar infection and other inflammatory diseases can produce transient electrocardiographic changes such as changes of the conduction time, increase of the duration of the electrical systole, flattening of the T-wave, pictures resembling infarction with negative coronary type T-wave. But we emphatically insist that our electrocardiographic interpretations will become much less lugubrious and infinitely more correct if we correlate certain electrocardiographic changes with radiologically observable changes in the size and shape and position of the heart. 'An appreciation of the dependence of the electrocardiogram on the size, shape, and position of the heart is absolutely fundamental', states Master (1939), 'in the interpretation of the electrocardiogram'. Alterations in the size, shape, and position of the heart, in the absence of any myocardial disease whatsoever, may produce changes in the cardiogram in every respect identical with those found in cases of myocardial damage. Our interpretation of the electrocardiographic changes in aortic stenosis may be recalled. At all events, we shall, perhaps, now understand why some patients that we sent to England with dismal diagnoses, substantiated by 'abnormal' cardiograms, were, to our surprise and possibly embarrassment, reported by the London cardiologist to have exceptionally sound and healthy hearts.

At the National Heart Hospital, Parkinson and Bedford (1928), whose experience in the correlation of electrocardiographic and radiological findings is quite unique, never failed to emphasize the fact that certain electrocardiographic changes may depend entirely on some alteration of the heart size, shape, or position and not at all on the myocardial state which may in fact be remarkably healthy. If these authors

(Continued at foot of next column)

## DIAMIDINO-STILBENE IN THE TREATMENT OF KALA-AZAR

By L. EVERARD NAPIER, F.R.C.P. (Lond.)

and

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By a process of incomplete experimentation and false deduction, it was concluded that certain guanidine derivatives, by virtue of their hypoglycæmia-producing properties, were capable of destroying the trypanosomes in experimentally infected mice. In attempting to confirm these observations, Lourie and Yorke (1937) found that insulin had no trypanocidal properties *in vitro* or *in vivo*, that *in vivo* one of these hypoglycæmia-producing compounds, namely

(Continued from previous column)

cannot afford to neglect such vital correlations, assuredly we cannot presume to do so.

In man there is no correlation between the heart rate and the shape and position of the heart nor between the heart rate and the electrocardiogram. In general, the heart rate is very rapid in small animals (600 p.m. in the mouse, 300 p.m. in the guinea-pig, 250 p.m. in the cat and 125 p.m. in the dog) and slow in large animals (55 p.m. in the horse and 46 p.m. in the elephant).

I am grateful to Lieut.-Colonel J. C. De, I.M.S., Principal of the Medical College and Superintendent of the Medical College Hospitals, Calcutta, for permission to publish this paper.

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synthalin, did not in fact produce hypoglycæmia except when given in doses sufficient to damage the liver, but that *in vitro* it had powerful trypanocidal properties.

This led to an investigation being undertaken under the auspices of the National Institute of Medical Research and the Liverpool School of Tropical Medicine (King, Lourie and Yorke, 1938) demonstrating the trypanocidal properties of a number of allied preparations, and later to another investigation by Dr. A. J. Ewins of Messrs. May and Baker on a series of aromatic compounds of the amidine group; amongst the latter 4:4'-diamidino-diphenyl ethylene was prepared.

Yorke (1940) used this preparation in the treatment of one case of kala-azar with apparently good results. The same writer also reported that other workers, including Dr. R. Kirk working in the Sudan, had had good results, but full details were not given.

One of the writers recently had an opportunity to discuss this subject with Dr. Warrington Yorke and at his request undertook to give a more extended trial to this drug in India. Meanwhile, Messrs. May and Baker had sent a generous consignment of 4:4'-diamidino-diphenyl ethylene (diamidino-stilbene, M.&B. 744) to the Director, Calcutta School of Tropical Medicine, for trial; this consignment he very kindly handed over to us.

This paper is a preliminary report on the results of this trial.

*The patients.*—Seven out of the eight patients who had a full course were Indian male patients in the hospital attached to the Calcutta School of Tropical Medicine. In each case the diagnosis of kala-azar had been made by the finding of leishmania in bone- or spleen-puncture material. The disease was of moderate duration, except in case 7 in which it was apparently of about 6 weeks' duration when treatment was started, and in case 4, in which it was of 18 months or more. Two other patients were attending the kala-azar out-patient clinic; one had a full course of eight injections and one ceased to attend after five injections, given on alternate days.

*The dosage.*—In our choice of dosage, we were guided by the clinical experience with this drug quoted by Dr. Warrington Yorke and by our own general experience that it is better to give as near as possible to the maximum tolerated dose at first, in order to ensure the maximum effect of the drug and establish its specificity (or the reverse, in which case it can be discarded immediately), and subsequently, if possible, to reduce the dosage, in order to find out the minimum effective dose, rather than to start too cautiously and in the event of failure to be uncertain if it is the drug or the dosage that is at fault. We therefore gave initial intravenous doses equivalent to 0.001 gramme per kilo body-weight. Though this dose was usually

tolerated without adverse symptoms, the patients became flushed, had a burning sensation all over the chest and abdomen, and slight dyspnoea, but these sensations passed off fairly rapidly. In a few instances the ill-effects were more disturbing (*vide infra*). We then increased this dosage slowly, usually by 0.01 g. (actual), up to 0.002 g. per kilo body-weight, but, as weights in our hospital are recorded in pounds, we subsequently first settled the maximum dose to be aimed at in each case, on the basis of 0.001 g. per pound weight, and then gave an initial dose of 0.050 g. (actual), if this was not more than two-thirds of the maximum dose, and increased the dose by 0.010 g. (actual) up to the maximum dose. We gave 8, 10, or 12 daily injections.

*Ill-effects.*—It is of interest that most of the ill-effects occurred in the first few cases treated and early in the treatment. Equivalent initial doses did not affect the subsequent patients, nor after tolerance had been established did subsequent larger doses in the same patient cause a repetition of the ill-effects.

The ill-effects amount to a marked exaggeration of the flushing and burning sensation mentioned above. One old woman with an oriental sore who was given a relatively very small dose (about 0.00025 g. per pound) became pulseless for some minutes, a second with kala-azar had severe burning and vomited, and future treatment was abandoned in both cases. A number of patients had rigors—these are noted on the charts. The symptoms were relieved almost immediately by adrenalin and in one patient, who had vomited on each occasion, a prophylactic dose of 0.125 c.cm. of adrenalin before the injection seemed to prevent the vomiting.

It was probably a coincidence that two patients developed pneumonia, one definite lobar pneumonia and the other, a child, bronchopneumonia, during, in one case, and, in the other, immediately after, the course of treatment. In both cases, M.&B. 693 was given and the condition cleared up in the usual way. Both of these patients had unusually high leucocyte counts, and the former had lung symptoms from admission.

One patient developed acute congestion of the conjunctivæ in both eyes with marked photophobia after the eighth and ninth injections; another injection was given, but the condition was not exaggerated. The eyes were normal again within a few days. No cause could be attributed, by the ophthalmologist, except an error of refraction; the fundus was normal.

In no instance did the treatment produce any psychological changes, nor did our patients exhibit the deplorable degree of moral turpitude reported by Dr. Kirk (Yorke, *loc. cit.*).

*Progress.*—It was unfortunate that many of the cases were in an afebrile phase when treatment was started. In cases 2 and 6, the temperature came down about the middle of the course of treatment. On the other hand, in other cases (*vide chart, case 7*) there was a distinct



reactionary rise and the temperature was maintained at a high level until the course was finished.

In all but the diabetes case the weight improved, in some considerably. Except in case 4 the spleen was markedly reduced and disappeared under the ribs so that at the time of discharge it could not be felt or could only be felt on deep inspiration. In case 4, there was little or no reduction after the first course, but after the second, it was more mobile and only about 3½ inches (originally 7 inches) below the costal margin.

The blood picture improved quite remarkably in every case; the red cell count and hæmoglobin showed a sharp rise despite the fact that no tonic or hæmatinic drug was given, and the leucocyte count was 8,000 or more in every case but two at the time of discharge.

**Proof of cure.**—This has always been a difficult problem. We have found (Napier, 1937) that immediately after the completion of an efficient course of neostibosan viable parasites could still be demonstrated in the spleen, but that in the course of a week or so they disappeared spontaneously, i.e., without further specific treatment; on the other hand, even when cultural methods have failed to show their presence, the patient has sometimes relapsed. Time alone is the test. However, some indication can be obtained from sternum puncture after a short interval and we did this in five of the eight patients; in one case parasites were still present 11 days after the last injection, and there is some reason to believe that this patient was not cured. In the other four cases, no parasites were found and it is believed that they were cured.

Data of the eight cases of kala-azar that had a full course are given in the table and temperature charts. A few further notes on each case are given below:—

**Case 1.**—Afebrile; abdomen distended and liver enlarged and tender. Spleen puncture was difficult on account of the distension and little material was obtained. Tibia puncture was done with a Salah needle and a good result obtained.

**Reaction.**—Flushing of the face only.

A few days after the last injection of M.&B. 744 was given the child developed pneumonia; this responded well to M.&B. 693 and the temperature was normal in 5 days; resolution followed, but the child's weight fell to 23 pounds. Subsequently he improved steadily.

**Case 2.**—A diabetic, incidentally the only case in our 20 years' experience at the School in which the two diseases have been seen in the same individual. His fever was of a high continuous type suggesting enteric.

**Reactions.**—Flushing of the face, burning sensation all over the trunk, dyspnoea, and slow and almost imperceptible pulse. Rigors after 0.050 and 0.060, but later tolerated 0.080 g.

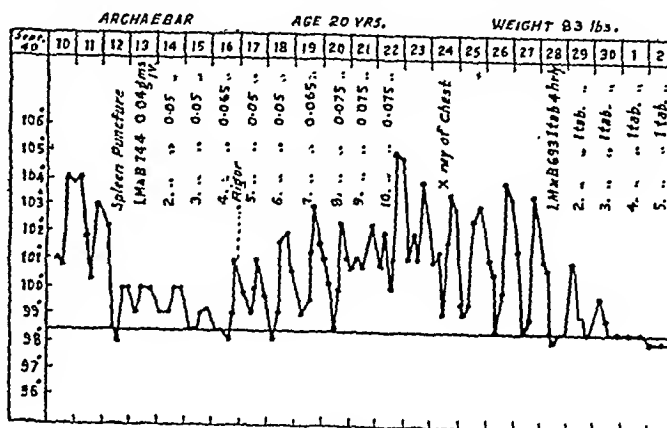
Insulin was not given during the treatment by M.&B. 744 and his blood sugar rose considerably.

Temperature fell after the second injection, but rose occasionally to 99.5°F., and was finally normal after the course was finished. He was a difficult patient and left hospital a week later.

**Case 3.**—Admitted with high fever, lung symptoms but without definite signs, and a slight leucocytosis.

**Reactions.**—Rigor after 0.065 g.

Temperature fell on the third day, but rose again and definite signs and symptoms of lobar pneumonia were noted on the 12th day. M.&B. 693, six tablets a day for 5 days brought the temperature down to



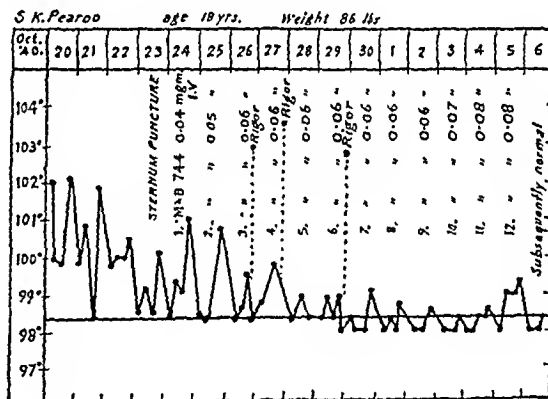
Case 3.

normal again (see chart). He improved rapidly but insisted on leaving the hospital.

**Case 4.**—A 'chronic' type of case; long duration, large hard spleen, and moderate intermittent fever.

**Reactions.**—Flushing, burning sensation, and rigors for the first few injections, later none.

Temperature fell to normal during the first course, but the spleen remained large and firm. Spleen puncture 11 days after the last injection showed leishmania still present but scanty. No fever during or after the second course; spleen still large, but softer and movable. His Wassermann reaction was positive at the time of admission.



Case 6.

**Case 5.**—Almost afebrile with respiratory symptoms but no physical signs.

**Reactions.**—Slight febrile reaction (100°F.) after first injection (0.05 g.), with flushing, burning sensation over abdomen, etc. No reaction after fifth injection (0.09 g.).

Temperature settled again to normal and remained so throughout.

**Case 6.**—A febrile case, moderately high remittent.

**Reactions.**—Rigors after 0.060 but later tolerated 0.080, also flushing and burning sensation.

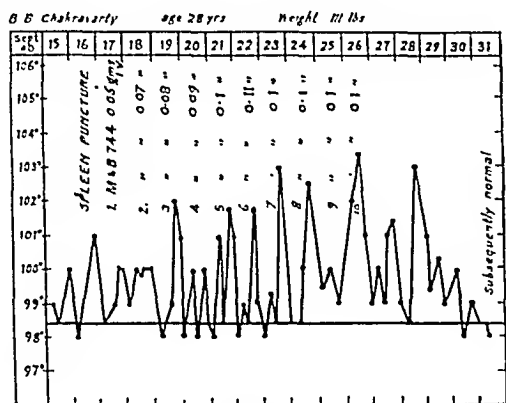
Temperature came down during the course, but was not finally normal until the injections were discontinued (see chart).

**Case 7.**—Admitted on the 14th day of fever of a high continuous type with clinical diagnosis of typhoid. The Widal was negative and the extremely low leucocyte count suggested kala-azar, but no parasites were found in the sternum-puncture material. Meanwhile, the temperature fell to normal, but the spleen showed signs of enlargement and after a month became puncturable, i.e., came down well below the costal margin. Leishmania were found.

**Reactions.**—Moderately severe when the higher doses were reached. His face became flushed, burning of the



body, severe headache, injection of the conjunctiva and photophobia which lasted for a few days. He had a sharp febrile reaction after each injection (*see* chart).



Case 7.

Case 8.—Treated as an out-patient; injections given three times a week.

Reactions.—Fairly severe reaction after the first dose of 0.014 g., subsequently no more reactions until the last dose of 0.020 g.

He was brought to the hospital for a week or so after the last injection and was considered to be cured by his guardians; his spleen was not palpable.

Other cases.—Three other out-door patients were treated—two cases of kala-azar and one a case of oriental sore. One boy received only seven injections and did not appear again. The other two were women and both had alarming symptoms after the first dose (*v. s.*) and on this account we decided not to undertake treatment amongst out-door patients, until we had had more experience with the drug. One patient, a boy aged 10 years, weight 61 pounds, with post kala-azar dermal leishmaniasis is still under treatment: up to the present he has received 20 daily injections totalling 0.950 g., maximum individual dose 0.060 g. (not well-tolerated). There is evidence of distinct improvement in the local lesions; under similar conditions treatment with an antimony preparation would not have produced any dramatic result.

Discussion.—We must emphasize the essentially preliminary nature of this report and in view of its incompleteness it is perhaps necessary to justify its publication.

Since antimony preparations were first used in the treatment of leishmaniasis in 1913, a very large number—the figure probably running into thousands—of antimony compounds have been prepared, some hundreds have been tested, and of these some dozens have been found to be efficacious; other drugs, which contained no antimony molecule, especially those which have proved useful in trypanosomiasis, *e.g.*, Bayer 205, and tryparsamide, and the all-conquering sulphonamides, have been tested in kala-azar, but up to the beginning of this year no drug that did not contain antimony has been proved to have any specific action in this disease, though from time to time hopes have been raised by apparent cures in one or two cases, or from the reports of inexperienced workers. The finding,

therefore, of a non-antimonial preparation that is effective in kala-azar is a matter, firstly, of considerable academic importance, and, secondly, one that may have far-reaching practical repercussions, for many obvious reasons of which not the least is that at the present moment the best antimony preparations are not available in the quantities in which they are required; therefore any claim to such a finding certainly demands confirmation.

Some of the difficulties of the clinical testing of anti-kala-azar drugs have been referred to above and have been discussed elsewhere by the senior writer (Napier, *loc. cit.*). The proper assessment of the relative efficacy of any drug necessitates a very extended trial—this writer's first report on neostibosan included 61 cases and his subsequent report 254. Though such an extended trial as this may not be warranted in this instance, it will in any case probably be a year or so before sufficient data have been collected to answer the many questions that arise, and therefore the expression of an interim impression seems to be called for.

The senior writer has, during the last 20 years, tested clinically in the treatment of kala-azar, under controlled conditions, in some thousands of cases, a very large number of preparations; of these many have been discarded and others have been selected and have taken their places in the pharmacopœias. He therefore feels that he is qualified, not only to carry out such an investigation on the comparative therapeutic value of this drug, but to express a tentative opinion on the drug before the stage where its full value, as compared with that of other drugs, has been accurately and scientifically assessed.

#### *Some of the questions that must be answered*

Very many questions remain to be answered, of which we mention a few.

The clinical progress in seven out of the eight cases who underwent a full course was extremely satisfactory and, from previous experience, we should expect most of them to be cured; the negative sternum-puncture findings add support to this expectation, but do not prove that cure has been effected. Time alone will show.

The dosage that we have been giving sometimes produces alarming symptoms, so that one could not advocate it, except under hospital conditions, and even under these one might encounter a hypersensitive patient in whom even more serious symptoms occurred. On the one hand, it is possible that we can find some means of obviating these symptoms, or, on the other, it may be necessary to adopt a lower standard of dosage. The former possibility is indicated by the fact that reactions have not been so severe or frequent recently as they were at first, and that in one or two cases a dose of adrenalin preceding the drug seemed to control the reactions.

Clinical experience with the drug has been so limited up to the present that its potentialities

Some of the bigger polyps contained a small amount of clear watery fluid which when expressed made these look quite flat. Histological examination showed the following:—

The papillomatous processes were obviously arising as proliferations of the Lieberkühn's glands which composed these polypoid masses (plate XXI, figure 2). Plate XX, figure 3, is a camera-lucida drawing of the section through a number of polyps with the whole of the thickness of the intestinal wall, and plate XX, figure 4, a single polyp of the bigger variety. These were seen to extend directly from the muscular coat. The submucosa was very scanty throughout the intestine and at places where the papillary projections appeared the submucosa was entirely absent (plate XXI, figure 2, and plate XX, figures 3 and 4). It seems probable that while the glandular proliferation extended into the lumen they also encroached on the deeper layers, thus causing the obliteration of the submucosa. The adenomatous character of these polypi are well seen in figure 2. No familial history could be traced.

**Case 2.**—Aged 30, was admitted into the hospital on 7th July, 1925, with the following:—

Constipation for eight days; no flatus was passed for five days; faecal vomiting for one day. On examina-

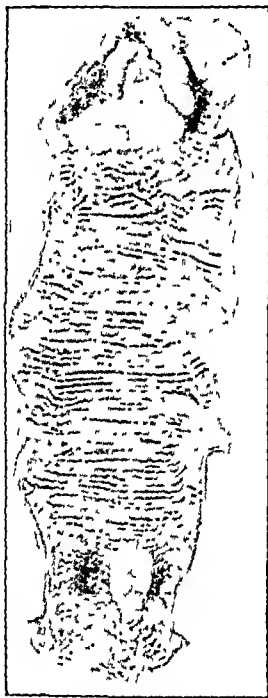


Fig. 5. Case 2.—Photograph of a piece of small intestine showing the two polypi. Note the irregular appearance of the growths.

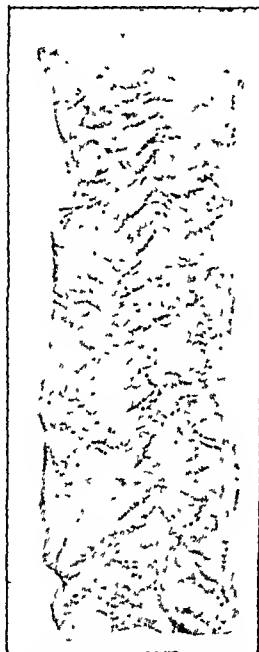


Fig. 9. Case 3.—Photograph of a piece of large intestine showing one polypoid growth with the slender stalk. A number of elevated areas in the mucous membrane are also seen.

tion, the abdomen was found to be soft but tympanitic; temperature 98.6°F. P/R = 100/36. Tongue was dry and he looked extremely toxæmic. High tube enema produced no result, nor did the compound enema yield anything. Stomach wash was given which showed the content to be faecal in nature. A laparotomy was performed and an intussusception was found in the small intestine about a foot from the ileo-colic valve. It was felt that a foreign body caused the obstruction which on examination was shown to be a polypoid tumour mass which was responsible for the intussusception. About two feet of the gut were resected with the polypoid growth. The patient expired six hours after the operation. The resected gut on examination was found to contain two polypoid growths which were situated about a foot apart from each other (figure 5). The topmost one was larger and was 1½ inches by 1 inch in

size. The mass was separated into four divisions by means of three fissures within it. The growth was found to arise from the intestinal mucosa by a small elongated stalk. The lower growth was about half the size of the upper one and was nodular in appearance. Several blocks were made from different portions of both the tumour masses and the following were made out:—

The tumours were composed of different types of structural patterns at different places. At certain places the mass was composed of tissue which was simply adenomatous in nature (plate XXI, figure 6). There was glandular hyperplasia, showing no malignant change. This sort of picture was predominantly present at the area from where the stalk of the polypi originated. plate XXI, figure 7, shows another type of composition of the tissue which consisted of normal glandular structure with a few glands showing atypical proliferation. In the deeper portion of the growth the tumour showed marked atypical proliferation of the glands which were evidently taking a malignant turn (plate XXII, figure 8).

**Case 3.**—Aged 12, was admitted into the hospital on 16th March, 1939, with a history of continuous fever for nine days. On examination the patient was found to be toxæmic and after four days' stay in the hospital he died of toxæmia and circulatory failure. The body was sent for post-mortem examination with a diagnosis of enteric fever. The autopsy examination showed a much enlarged spleen, weighing 920 grammes, and a number of ulcerated areas in the jejunum and ileum. The character of these ulcers was like that of enteric ones. The large intestine, at the sigmoid part, showed a number of polyps. Besides these there were areas in the large intestine which showed slight nodular elevation in the mucous membrane (figure 9). Some of these areas looked just as prominences from the mucous surface, others presented distinct elevations. Histological sections from different portions of the elevated areas and the polypoid growths showed the following:—

The elevated areas showed slight adenomatous change in the simple tubular glands of the mucous membrane (plate XXII, figure 10). The definite polypoid growths on section showed very marked hyperplasia (plate XXII, figure 11) and sections from the deeper portions of the tumours showed frankly precancerous condition (plate XXII, figure 12).

### Comments and discussion

Multiple adenomata and malignant adenomata of the large intestine are two different pathological entities. Lockhart-Mummery (1935) has pointed out the difficulty of accepting such clear-cut divisions to differentiate between the two types and he has suggested the name adenomatosis, where numerous small polypoid growths occupied practically the whole of the large gut. This extremely rare disease has also been described as multiple adenomata and colitis polyposa. The condition has distinct familial predisposition. Our case 1 is an instance of such a condition; although the family history was not available the picture (figure 1) is a typical one. The patient had the first symptoms about six months before his death. It can be assumed that the lesion might have started earlier, yet the extensive nature of the involvement and the uncountable number of polyps clearly show the extreme rapidity with which the disease progressed. The histological picture of the individual growths did not suggest any malignant change (plate XXI, figure 2). We studied histological characters of the polyps of all the



Fig. 3. Case 1.—Camera-lucida drawing of a section of a piece of tissue showing a number of polypi with the intestinal wall. Note the finger-like projections of the adenomatous condition; some of these are overlapping each other leaving no healthy area.



Fig. 4. Case 1.—Magnified camera-lucida drawing from a section of the intestine showing a single polyp entirely. Note the absence of the submucosa. The adenomatous structure is sharply limited by the muscular layer which shows no change.





Fig. 2. Case 1.—Photomicrograph of the section of a piece of tissue from the intestinal wall; at one corner of the picture a small strip of the muscular coat can be seen; the rest of the picture is composed of the adenomatous structure. The submucous coat is practically obliterated.  $\times 150$ .

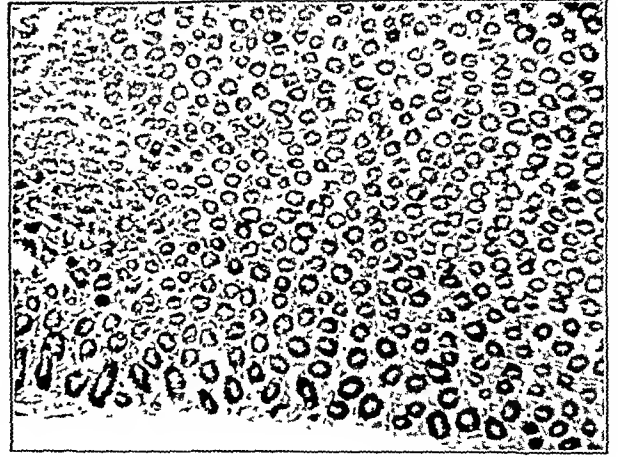


Fig. 6. Case 2.—Photomicrograph of a piece of tissue from the base of the growth. The adenomatous condition is evident.  $\times 150$ .



Fig. 7. Case 2.—Higher power photomicrograph showing the transition from the stage of simple adenoma to malignant change. Note the group of glands at the centre. These are different in nature from the normal ones and represent the initial stage of the malignant forms.  $\times 340$ .



Fig. 8. Case 2.—Photomicrograph of a piece of tissue from the deeper portion of the tumour showing mostly adenocarcinomatous processes; besides there are hyperplastic normal glands and a few transitional ones.  $\times 210$ .



Fig. 10. Case 3.—Lower power photomicrograph of a piece of large intestine from the elevated area. Note the normal glandular appearance and the simple adenomatous change in the same field.  $\times 150$ .



Fig. 11. Case 3.—Higher power photomicrograph to show the simple glandular hyperplasia taking malignant change. Note the gradual change from the benign to the malignant form.  $\times 210$ .

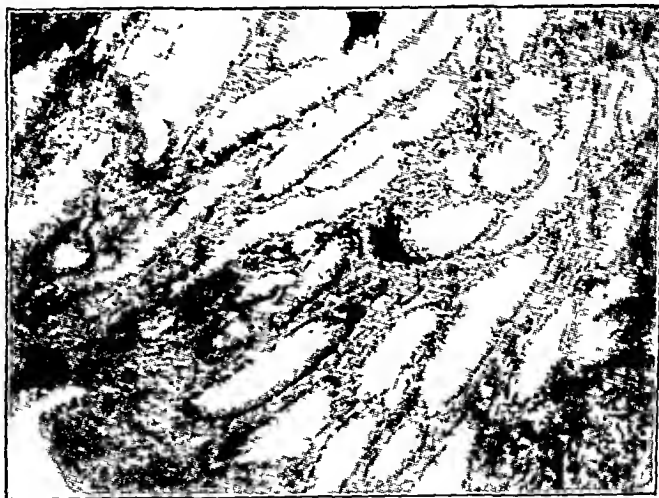


Fig. 12. Case 3.—High power photomicrograph of the tissue from the deeper parts of the polyp. The malignant nature of the growth is evident.  $\times 240$ .



sizes, but the nature of the growth was essentially the same everywhere, viz, simple adenoma. In the bigger polyps the growth varied only in quantity. It could be seen that the polypoid growth was sharply limited by the muscular layer (plate XX, figures 3 and 4), the submucosa being almost completely encroached by the growth. Although the individual growths were benign in nature histologically, the sum total effect of all these produced results which were far more injurious than that can be caused by simple irritation. The collection of mucus and cellular exudate and the faecal matter in between the different polyps gave the intestine a rigid structure and the finding at the rectal examination thus could be easily explained. Cases 2 and 3 are of course quite different in nature from case 1. Case 2 showed adenomatous polypi in the small intestine and case 3 in the large intestine. By studying a number of blocks from different parts of the tumours in both these cases, the transition from simple glandular hyperplasia to atypical proliferation could be made out. Plate XXI, figure 6, and plate XXII, figure 10, show a simple adenomatous condition. From this simple adenomatous condition a number of glands lying side by side with normal ones are clearly seen to assume an atypical nature (plate XXI, figure 7, and plate XXII, figure 11). This clearly shows the malignant tendency of these glandular structures. At other areas the normal appearance of the gland have almost disappeared (plate XXII, figure 8, and plate XXII, figure 12) assuming an appearance of malignancy. The question naturally arises whether these cells which are taking a malignant turn are simply transitions from normal structures or whether these particular cellular elements were endowed with a genetic capacity for malignant proliferation which was dormant but suddenly let loose later? This naturally takes us to the various theories as to the mode of production of new growths.

#### Summary

Three cases of intestinal polypoid condition are described, of which two cases occurred in the large bowel and one in the small intestine. One case was found to be a condition of multiple adenomatosis, a very rare condition, and two cases showed the pictures of simple adenoma of the mucous membrane showing malignant change.

In conclusion, our thanks are due to the Superintendent, Medical College Hospitals, Calcutta, for the case records and to the members of the staff of this department for the help rendered.

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## ECTOPIC PREGNANCY

### (A CLINICAL NOTE)

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SINCE Albucasis in the eleventh century first described extra-uterine pregnancy, a great deal of literature has accumulated on this subject. Nature has so arranged matters that the embryo of the human race is from an early date accommodated in and fed from the uterus. It would therefore seem reasonable to suppose that its conception should also take place there. However, this appears not to be the case; probably on account of the difficulty of transport for the delicate ovum. It is now established, practically beyond all doubt, that the human ovum is normally impregnated within the lumen of one of the fallopian tubes most usually at the fimbriated end.

Ovulation takes place about the 14th day of the menstrual cycle, counting the 1st day of the period as the 1st day of the cycle. The ovum, still surrounded by its zona pellucida, is extruded through the rupture of the graafian follicle and lies free near the surface of the ovary. The latter is in close apposition to the fimbriated end of the fallopian tube which attracts the ovum towards its open ostium. (The exact method of the entrance of the ovum into the tube is still unknown.) When the ovum enters the abdominal ostium of the tube, it is probable that the latter closes and is sealed by the enfolding action of the fimbriae. The ovum is now ready for impregnation, but, if this does not occur in 2 days, it dies, the corpus luteum undergoes necrosis, and the phenomenon of menstruation results.

If however the ovum is destined for impregnation, the procedure is as follows:—

The seminal fluid on ejaculation is deposited in the neighbourhood of the external os of the cervix uteri, and in the posterior vaginal fornix. At once the sperms begin to make their way through the cervical canal, and the uterine cavity, into the tube, and finally one fuses with the ovum usually in this fimbriated end. From all accumulated evidence it appears that only those sperms deposited in or around the external os are available for impregnation, and that the 'vaginal pool' (Adair, 1940) in the posterior vaginal fornix is merely excess. Sperms which are deposited in this pool are very short-lived owing to the acidity of the vaginal secretions which is inimical to them. Indeed sperms acted upon by the normal acid vaginal secretion may lose their motility in less than half an hour. Very rarely the ovum is impregnated in the ovary in the graafian follicle, giving rise to an ovarian gestation, only some 40 genuine cases of which have been reported up to 1927 (Eden and Lockyer, 1935).

Impregnation in the abdominal cavity has never been authentically reported though it has

been suggested. It is estimated that the sperms travel at such a pace that fertilization takes place within a few hours of coitus. Therefore coitus during the 10th to 15th day of the menstrual cycle is the most likely period in which to effect impregnation, *i.e.*, the 'dangerous period'. This is a much truer dictum than that of the opposite end of the cycle, *i.e.*, the so-called 'safe period'.

Normally, on fusion with the sperm, the impregnated ovum makes its way through the tube into the uterus and becomes embedded in the engorged endometrium which has been got ready for it. Therefore, it stands to reason that any factor which causes delay in this migration will favour the continuance of the pregnancy at the spot where the delay occurs, for the sperm being much smaller than the ovum can pass through a narrower lumen, and consequently any inflammation, kinks or adhesions which cause a partial stenosis of the tube may prevent the passage of the ovum. Some authorities state that, as long as the zona pellucida remains intact, the embedding of the ovum in the tube cannot take place. Therefore, anything which gives rise to premature shedding of this membrane favours a tubal pregnancy. The tube, being composed of tissue very different to that of the uterus, cannot dilate to accommodate a pregnancy of more than a few weeks, so that the onset of symptoms occur which, if neglected, may lead to rupture of the tube from over-dilatation. Rupture may also be caused by the eroding action of the trophoblast which is much more serious in the tube than in the uterus.

The fimbriated end of the tube is more dilatable than the uterine end, so that symptoms, or rupture, are more likely to occur early if the pregnancy is situated at the isthmus. Rupture of the tube in tubal gestation of the ampulla usually does not occur until towards the end of the second month, whereas it may take place in the first 2 or 3 weeks if the gestation is in the isthmal portion. This is an important point and is one which calls for accurate diagnosis of the situation of the pregnancy, on account of the urgency in undertaking operative interference at an early date.

The following case history is an example:—

Age 24, married 13 years: one child, seven years old. The patient was admitted at 12 noon on 19th July,



1939, as an acute emergency. The following history was available. Severe pain in the lower abdomen, and  
(Continued at foot of next column)

## PROLAPSE OF THE RECTUM IN CHILDREN AND THE ROLE PLAYED BY GALLOWS SPLINT IN THE CURE OF THIS CONDITION

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PROLAPSE of the rectum is common both among adults and children. Among adults it is common after the 4th decade and in children between the ages of 2 and 4. Males were more commonly affected than females, and among children the ratio of male to female children was 9:1 in a total of ten cases treated so far. In none of the cases of prolapse of rectum among old people, could they give a history of prolapse in early life, as is stated in the textbooks. It is possible that the class of people who were suffering from this disease could hardly remember their past history and the question is still an open one. In children, however, it is common owing to bad hygiene, dietetic errors, and gastrointestinal infections. The prolapse in children may be complete or partial. In cases of partial prolapse, polypus is often the cause of this condition and these cases are brought to the hospital with a history of bleeding before,

(Continued from previous column)

some slight vaginal bleeding for last five days. Periods had been quite normal and regular, the last one about a month ago. The patient stated she was expecting her next period at any moment. Early that morning the patient suddenly got worse, so she was brought to hospital.

*On examination.*—She was pulseless, blanched, and collapsed. The abdomen was tense and swollen. The case was obviously one of intra-abdominal bleeding, probably from a ruptured ectopic. The patient was brought to the operating theatre at once and the abdomen opened. On incising the peritoneum free blood was seen in such quantity and under such tension that it spouted up into the air. As much as possible of this, about 16 ounces, was caught in a sterile bowl in which was a solution of sodium citrate, and this was given to the patient as an intravenous auto-transfusion during the operation. At first it was not clear where the bleeding was coming from, as no tumour could be felt, and the fimbriated ends of both fallopian tubes were seen. A rapid inspection of the spleen and other organs did not reveal any injury, so the blood was then swabbed out of the cavity with great rapidity when the small rupture at the isthmal end of the right tube was apparent (*vide illustration*). The bleeding was coming from a spouting vessel at the medial aspect of the rupture. The tube was removed in the ordinary way and the patient made an uneventful recovery.

My thanks are due to Dr. B. P. Tribedi, the Professor of Pathology in the Medical College, for the drawing of the specimen.

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during, or after the motion. Sometimes the bleeding is of an alarming character, and frequent hæmorrhages cause anæmia and debility. In these cases removal of polypus cures the prolapse and improves the general condition of the patient. In cases of complete prolapse the mothers of the children generally seek admission with a history of dysentery or diarrhœa. On admission, the children are found to be emaciated with a complete prolapse, this in some cases being irreducible with marked œdema (figure 1). The problem of treating these



Fig. 1.—Complete prolapse in a child with œdema causing irreducibility.

children as out-patients is difficult, because the home condition of the majority of the people who seek advice is very poor. It is therefore necessary to hospitalize these cases.

The whole principle of treatment of this prolapse is :—

- (1) to reduce the prolapse and maintain it reduced,
- (2) to attend to the dietetic errors, and
- (3) to treat the infective condition of the intestinal tract which preceded the prolapse.

The reduction of prolapse in the majority of the cases is easy, but maintenance is difficult. The mode of evacuation either by sitting on a commode or in the usual way the Indian children defæcate is inimical to the cure of this condition. The following scheme has given satisfactory results :—

- (1) Both legs are slung up in a gallows splint, as in treating a fracture of the femur, so that the buttocks are slightly raised from the bed and the glutei strapped (figure 2).
- (2) The motion is examined for amœbæ and other infections, and, if present, treatment is given for this infection.
- (3) Diet is regulated and deficiency of vitamins supplied.

It is important that the child should have the motion lying in bed. This is the essential part of the treatment and this object is gained by using the gallows splint. The use of this splint perforce prevents the child from getting up and provides the rest that is so necessary for the children who are debilitated. To facilitate an

easy soft motion, the child is given liquid paraffin at night and a paraffin enema of 2 to 3 ounces through a rubber catheter high up in the rectum in the morning. With this simple treatment the prolapse becomes easily reducible and when reduced remains inside without recurrence. This method of postural evacuation prevents the straining and the lubrication of the bowel produces a soft motion in bed, preventing its recurrence. The child is kept in this splint for a minimum period of a fortnight during which time it picks up weight and general health, and thus cure is obtained. Ten



Fig. 2.—The child in the gallows splint with extension of limbs and reduction of prolapse, ten days after the institution of treatment. Note the general well-being of the patient

children with complete prolapse were treated in this way and all the children had a cure at the time of discharge and on follow up four have reported no recurrence, two have died due to other diseases and four have not replied due to improper address and other causes.

### Conclusion

The essential part of the treatment is reduction of prolapse and to maintain it reduced until the general condition is improved and the cause dealt with. The use of gallows splint has contributed to the rapid cure of this condition and has proved useful for the following reasons :—

- (1) It necessarily confines the child to bed.
- (2) It gives complete rest which is so necessary in debilitated children.
- (3) Raising of buttocks helps in the reduction of congestion associated with prolapse and thus helps in its reduction and prevents recurrence.
- (4) It facilitates nursing and especially the use of bed-pan for an easy evacuation without disturbing the child.

## SMALLPOX AND SULPHONAMIDE

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*Introduction*

SMALLPOX is primarily a disease of children, but the introduction of protective vaccination in early childhood has resulted in the greater prevalence of the disease among the adult population.

In Bombay, we have a large floating population who migrate periodically from rural areas in search of employment and these constitute the bulk of our labouring class.

TABLE I

Compiled from hospital records for the years 1923 to 1939\*

Age period	VACCINATED		UNVACCINATED	
	Cases	Deaths	Cases	Deaths
0-5 ..	181	6 ( 3.3%)	1,085	457 (42.1%)
5-10 ..	232	8 ( 3.4%)	474	84 (17.6%)
10-20 ..	2,527	93 ( 3.7%)	1,529	429 (28.0%)
20-30 ..	2,839	203 ( 7.1%)	1,867	859 (46.0%)
30-40 ..	599	44 ( 7.3%)	491	225 (45.8%)
40-50 ..	115	19 (16.5%)	97	58 (60.0%)
50 and upwards	62	13 (21.0%)	51	29 (57.0%)

\* Data taken from the Annual Reports of the City Fever Hospital, Arthur Road, Bombay, from 1923 to 1939.

This table is instructive in that it points to some important deductions, namely, (i) among the vaccinated the immunity wears off by the 10th year; (ii) the unvaccinated have a heavy mortality should they contract the disease;

(iii) mortality among the vaccinated is considerably less, as compared with the unvaccinated.

In Bombay, we have smallpox with us every year; during some years the disease assumes epidemic proportions.

*Hospital cases*

Cases that are admitted into this hospital are from the poor labouring class and usually from the adult population. A good proportion of these cases seek hospital treatment only when the disease is in advanced stage.

*Classification of smallpox cases*

Cases which are admitted for treatment are grouped clinically under four types, namely, the discrete, the semi-confluent, the confluent, and the hæmorrhagic.

This table shows that under hospital treatment the mortality among the discrete cases is negligible; the confluent type has a mortality of about 47 per cent and this is due to the fact that these cases develop a septic stage from which many succumb. The hæmorrhagic type has the highest mortality, 88 per cent.

In the discrete type, the deaths that occur are due to pneumonia. In the semi-confluent type, deaths occur only in those cases which develop sepsis, and the mortality varies from 4 to 20 per cent. In the confluent type the deaths are mainly due to sepsis. The stage of suppuration is usually on the 7th or the 8th day of the disease, and the patient succumbs to septicæmia or toxæmia. The infecting organism in the majority of the cases is the staphylococcus, but in some cases streptococci are also found. Specific treatment with vaccines and sera has not been a success. This type may be further subdivided into two varieties; in one the rash is flat instead of being raised and prominently projected; in the other the rash presents the usual characteristics. The hæmorrhagic type is the most severe manifestation of the disease;

TABLE II

Compiled from hospital records for the years 1930 to 1939

Years	DISCRETE		SEMI-CONFLUENT		CONFLUENT		HÆMORRHAGIC	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
1930 ..	559	6	308	18	224	83	204	169
1931 ..	14	0	4	0	5	2	6	4
1932 ..	136	0	80	1	37	15	49	44
1933 ..	1,130	4	436	33	294	138	257	236
1934 ..	57	0	50	1	30	18	26	21
1935 ..	361	0	232	8	214	78	114	99
1936 ..	217	0	275	9	139	62	79	67
1937 ..	286	0	193	5	144	94	28	27
1938 ..	837	0	305	3	398	199	131	121
1939 ..	106	0	56	3	32	21	16	15
10 years ..	3,703	(0.2%)	1,939	(4.1%)	1,517	(46.8%)	910	(88.2%)

in this also, we have noted two forms; in one the hæmorrhage occurs from the onset of the disease, and the rash is of the purpuric variety while there are hæmorrhages from the mucous membranes of the conjunctiva, mouth, etc. It is also attended with hæmaturia, melæna, hæmoptysis and hæmatemesis. The patient usually succumbs within 7 to 10 days of the onset. In the other variety hæmorrhage is not seen until after the rash has fully developed; it is then found in the pox. This type has been described as hæmorrhagica pustulosa. These cases have been treated in the past with serum from convalescent cases; the results have not been encouraging, as the mortality among the treated was nearly the same as in the control cases.

*Researches into the treatment of confluent and hæmorrhagic cases*

In 1924, 25 cases of the hæmorrhagic type were treated with convalescent serum and the results were not encouraging; the late Dr. Patel considered that 'the antitoxins in 20 c.cm. of the convalescent serum are probably not enough to neutralize all the toxins in the body'.

In 1933, some selected cases of the confluent and hæmorrhagic types were treated with sera obtained from calves used for the preparation of vaccine lymph at Belgaum, serum obtained from locally immunized sheep, and serum from convalescent patients.

TABLE III

Treatment	Cases	Deaths	Controls	Deaths
Calf serum ..	20	15	20	14
Sheep serum ..	2	2	2	2
Convalescent serum	25	20	25	18

During the same year, confluent and hæmorrhagic cases were exposed to the rays of Vitalux lamp for varying periods from 5 to 30 minutes according as the patient could bear the heat. These rays had definite result in drying up the pox earlier than usual in the septic stage.

During the year 1938-1939, some selected cases of the septic confluent type were treated with sulphonamide and uleron administered orally.

TABLE IV

Treatment	Cases	Mortality, per cent
Sulphonamide .. ..	125	25.0
Uleron .. ..	19	32.0
M & B. 693 .. ..	16	37.5

Uleron seemed to be definitely toxic in the doses administered; some of the cases were treated with M.&B. 693 in the early eruptive stage, before the development of pustules. It

neither aborted the eruptive stage, nor did it prevent the development of the pustular stage. Sulphonamide seemed to be effective in the treatment of the late septic manifestations such as septicæmia, arthritis, furunculosis and in lung complications.

*Sulphonamide and confluent smallpox*

Results obtained with sulphonamide in the selected cases treated during 1938-1939 justified a further trial with the drug during this year with adequate controls.

From January to May 1940, we have treated 91 cases of the semi-confluent type with 64 controls and 60 cases of the confluent type with 63 controls. In June there has been a great drop in admissions for smallpox. As one of us (T. B. P.) has taken up a new post it seemed desirable that the results we have obtained be summarized in order that others engaged in the treatment of smallpox may give further trial to this drug, so that in course of time a successful way of dealing with the confluent type of smallpox may be evolved.

The sulphonamide group of drugs have established their therapeutic value in the treatment of diseases such as cerebrospinal fever, pneumonia, gonorrhœa and puerperal fever. It is claimed that the drug is specific against organisms of sepsis, staphylococci and streptococci. Our results in the treatment of confluent cases of smallpox justify the use of this drug.

TABLE V

*Summary of cases treated with sulphonamide during January to May 1940*

	Treated	Mortality, per cent	Controls	Mortality, per cent
Semi-confluent cases:				
Vaccinated	59	18.6	32	28.1
Unvaccinated	32	18.7	32	34.4
Confluent cases:				
Vaccinated	32	50.0	30	93.3
Unvaccinated	28	64.3	31	93.5

These figures are admittedly small, but that sulphonamide does exert a beneficial action is clear.

We have employed sulphonamide tablets sold by Parke, Davis & Co. and by Glaxo Laboratories. Two tablets were administered orally at four-hourly intervals for the first 7 days; thereafter one tablet was given four-hourly for the next 7 days. The maximum amount administered varied from 44 to 47.5 grammes. In a very large number of cases the amount of the drug administered was small, as the drug was withheld as soon as the temperature reached normal.

During the administration of sulphonamide we have observed very few untoward symptoms:

(Continued at foot of next page)

TABLE II

	Day of fever	H-agglutination	Vi-agglutination	REMARKS
Case 8	8th day	— 25	+ 25	Clinically enteric.
	15th "	+200	+100	
Case 9	30th day	— 25	+ 25	<i>B. typhosus</i> (Vi strain) was isolated on the 30th day. Relapse?
	39th "	+200	+100	
Case 10	7th day	— 25	-- 10	<i>B. typhosus</i> isolated from blood on 7th day.
	20th "	Not done	+ 50	
Case 11	7th day	— 25	+ 50	<i>B. typhosus</i> isolated on the 7th day.
	After 9 weeks when the patient had fully recovered from the fever.	Not done	+ 25	
Case 12	8th day	— 10	+ 50	Clinically typical enteric.
	24th "	Not done	+200	
Case 13	14th day	— 10	— 10	<i>B. typhosus</i> isolated.
	21st "	+200	+ 25	
Case 14	11th day	— 10	— 10	<i>B. typhosus</i> isolated. This strain agglutinated with Vi serum, 'H' and 'O' sera
	24th "	— 10	+ 50	
Case 15	13th day	— 10	+ 10	Clinically enteric.
	24th "	— 10	— 10	
Case 16	18th day	+200	+200	Clinically enteric.
	22nd "	Not done	+400	

Statistical note by Mr. Sastri, statistician of the University of Madras

	Positive reactions	Negative reactions	Total
Vi-agglutination	202	53	255
H-agglutination	160	95	255

Proportion of positive reactions in Vi .. 0.7922  
Proportion of positive reactions in H .. 0.6274  
Difference .. 0.1648

Standard error of the difference :  
 $\sqrt{\frac{0.7922 \times 0.2078 + 0.6274 \times 0.3726}{255}} = 0.0395$

Therefore,  $\frac{\text{Difference}}{\text{Standard error of difference}} = \frac{0.1648}{0.0395} = 4.172$

Hence, the difference is highly significant and in detection Vi-agglutination is superior to H-agglutination.

Positive reaction

	Vi-agglutination	H-agglutination
Enteric fever cases	202	160
Non-enteric fever cases.	12	5
	214	165

Out of the 214 cases giving positive reaction by Vi method, 94.4 per cent had enteric fever.  
Out of 165 cases giving positive reaction by H-agglutination method, 97.0 per cent had fever.  
We have to find out whether the difference between the two proportions is significant or not, to test whether

one of the methods is more efficient in making correct diagnosis than the other.

Standard error of difference:

$$\sqrt{\frac{0.944 \times 0.56}{214} + \frac{0.970 \times 0.030}{165}} = 0.021$$

Therefore,  $\frac{\text{Difference}}{\text{Standard error}} = \frac{0.026}{0.021} = 1.238$

Hence, the difference is not significant. From this we cannot say that the specificity of H-agglutination is superior to Vi-agglutination. But it must be noted that the number of non-enteric cases is too small compared with enteric cases.

Acknowledgments

We are indebted to Dr. C. G. Pandit, Acting Director, King Institute, and to Lieut.-Colonel H. E. Shortt, I.M.S., Director, King Institute, Guindy, for their encouragement, to the latter also for helpful suggestions and criticism in the preparation of this paper. Our thanks are also due to the superintendents of the Government Royapuram, Government Royapettah, Government Victoria Caste and Gosha and Government Women and Children Hospitals for their permission to make use of the clinical material. We are also thankful to Dr. S. Venkatasamy of the King Institute, Guindy, for his assistance in this investigation.

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## EXISTENCE OF LEPTOSPIROSIS IN RANGOON

By B. M. DAS GUPTA

(From the Protozoology Department, Calcutta School of Tropical Medicine)

TAYLOR and GOYLE (1931) found in Rangoon that out of 100 *Nesokia bengalensis* examined 42 were infected with leptospira, while among the house rats, *Rattus rattus* and *R. concolor*, 23 showed the infection. They also noted that a rat strain isolated in Rangoon corresponded with a Sumatra rat strain, but not with human strains isolated by these workers in the Andamans.

There is little doubt that human leptospirosis also exists in Burma, although there is, as far as I am aware, no published record of the occurrence of the disease\*.

In July 1939, Lieut.-Colonel G. C. Maitra, I.M.S., the then Director of the Pasteur Institute, Rangoon, sent to me a specimen of serum from a case of jaundice with a request to perform an agglutination test for evidence of leptospiral infection. The serum was put up against the different strains of leptospira then available in my laboratory.

TABLE I

Strains	SERUM DILUTIONS			
	1-20	1-40	1-80	1-160
Strain Chopra, Calcutta (classical <i>L. icterohæmorrhagiæ</i> ).	+	+	+	+
Strain Wijnberg (classical <i>L. icterohæmorrhagiæ</i> ).	+	+	+	+
Strain Andamans CH31	—	—	—	—
Strain Andamans CH11	—	—	—	—
Strain Mg. Tin Tin*	+	±	—	—

\* This strain was isolated by me from an Andaman case; homologous with a Java bat strain, 90C.

In order to obtain the limit of agglutination, further dilutions were made as follows:—

TABLE II

	1-1,000	1-10,000	1-100,000	1-1,000,000
Strain Chopra	+	+	+	±
Strain Wijnberg	±	—	—	—

It is evident from the results presented in the above tables that the serum was obtained from  
(Continued at foot of next column)

\* Since this paper was sent to the press, I have come across a reference to the occurrence of leptospiral jaundice in Rangoon in the 'Annual Report of the Burma Pasteur Institute and Bacteriological Laboratory for the year ending 31st December, 1929, and the 31st March, 1930, respectively'. The serological nature of the causal organism was not, however, determined.

## RABIES IN LOWLIER ANIMALS

By S. D. S. GREVAL

LIEUTENANT-COLONEL, I.M.S.

The School of Tropical Medicine, Calcutta  
and

M. J. NICHOLAS, I.M.D.

The Pasteur Institute, Calcutta

### Advice in a case of tortoise bite

A RESIDENT of 'A' in the United Provinces was bitten by a tortoise while bathing in the river. Advice regarding anti-rabies treatment was required at Calcutta by a relative on 17th October, 1940.

Tortoises do not usually bite bathers in rivers. Two questions arose—Was there anything wrong with this particular tortoise? Had anybody at 'A' ever heard of a case of rabies in man or animals after a tortoise bite? These questions could not be answered satisfactorily by the relative. The advice given was that the treatment should be taken if the biting animal had behaved in an obviously unusual manner and if cases of rabies in man or animals were known to have occurred from bites of tortoises.

### Rabies in the tortoise

There is no mention in the available literature on the subject, in English or French, of naturally-occurring rabies in tortoises. Street virus, however, has been injected into brains of turtles and proved by passage into rabbit brain to have persisted for months. In the brains of *Testudo mauritanica* and *Clemmys leprosa* (a fresh-water species) it persisted for 302 and 150 days, respectively (Remlinger and Bailly, 1931, 1932). The turtles did not show any sign of rabies.

The difference between turtles and tortoises is not sharp. That a tortoise can acquire infection in nature, remain healthy and impart infection by bite are possibilities. Identical occurrences have been observed in bats.

Incidentally, 'unusual' behaviour may and actually does fall short of signs of rabies and yet is a very useful guide in rabies. When during a hunt jackals turn on the hounds they behave unusually. Rabies in the pack usually follows.

(Continued from previous column)

a case of leptospirosis and the infecting organism was homologous with the classical *L. icterohæmorrhagiæ*.

My thanks are due to Lieut.-Colonel G. C. Maitra, I.M.S., Director, Pasteur Institute, Rangoon, for sending me the material on which this note is based.

### REFERENCE

Taylor, J., and Goyle, A. N. (1931). *Indian Med. Res. Mem.*, No. 20. Thacker, Spink and Co., Calcutta.

Local information regarding incidence of rabies, specially from small localities, is very valuable. The impression produced by the actual suffering of this rare catastrophe and by the hopelessness of the situation is retained by the inhabitants for a long time.

#### *Rabies in other lowlier animals*

Other lowlier animals which have been experimented upon are the hedgehog (*Eurinaeus europaeus*) and the spermophile (*Spermophilus citellus*). The spermophiles were resistant during hibernation. The hedgehogs, on the other hand, transformed the fixed virus into the street virus (Jonnesco, 1932). The latter experiment would show that the hedgehog was particularly suitable to be a host of rabies virus. It may be one of the natural reservoirs.

Zoologically hedgehogs and spermophiles being mammals are above tortoises which are reptiles. In popular language, however, all of them are lowlier animals amongst the lower animals.

Attention has been recently drawn to bats, some of which have definitely been proved to carry rabies and others are, therefore, under suspicion (Greval and Nicholas, 1940). The bats are also lowlier animals.

Attention was also drawn to rabies in the mongoose (Greval, 1932, 1933). The mongoose, however, is a carnivore and ranks with the dog which is not a lowlier animal.

#### *Natural reservoir of rabies*

One of us (Greval, *loc. cit.*) has suggested that like the fire in ancient India, before the introduction of matches, rabies smoulders in forests and flares in human habitations. The smouldering probably occurs in the wild carnivores which do not always die of it. It is now suggested that it may occur even in the lowlier animals which may not be much inconvenienced by it. It is not in the best biological interest of a parasite always to cause lethal infection, *e.g.*, rabies in lower animals and man. Such an infection would exhaust the supply of hosts in time and thus terminate the existence of the parasite.

#### *Danger of anti-rabies treatment*

In taking the treatment there is a risk of developing the post-treatment paralysis. The paralysis, however, is a rare event and the risk must be preferred to certain death, should rabies develop as a result of the bite. Besides, the majority of cases of paralysis, definitely attributable to treatment, which have come to the knowledge of the writers during the last 19 years, have completely recovered. During the last six years, out of 35 cases reported from the various anti-rabies institutes of India and Burma only 7 proved fatal.

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(Continued at foot of next column)

### ON USING WATER INSTEAD OF DUST FOR DILUTING PARIS GREEN IN MALARIA CONTROL\*

By PAUL F. RUSSELL

FRED. W. KNIPE

and

T. RAMACHANDRA RAO

In another report (Russell and Jacob, 1939), one of us referred in passing to the use, at our field station, of a dustless method of diluting Paris green based, with modifications, on that recommended by Barber *et al.* (1936). After two years' successful experience with this modified procedure in Pattukkottai taluk, we believe a report may be useful, for the measure appears to us to have great value in India.

#### *Technique*

First, the following stock suspension was prepared:—

#### *Stock suspension*

Kerosene oil (Elephant brand—		
Socony)	..	400 c.c.
Paris green	..	200 c.c.
Egg albumin, dry, powdered, commercial	..	1 gramme†

The above ingredients were added, in the order mentioned, in a Winchester bottle holding 3 litres and thoroughly shaken. (The total volume will be found to be 480 c.c.m.) For convenience, separate tins of definite volume were used for measuring out kerosene oil and Paris green. The latter can be measured easily in a tin and, if quite dry, can be poured. The stock suspension must be thoroughly shaken every time some has to be poured out. (No water for mixing with egg albumin is being used, as after repeated tests it was found that it tended to make the stock suspension coagulate so that it was then impossible to keep the Paris green floating.)

In the laboratory, a number of glass vials—shell vials, 4 inches  $\times$  1 inch, with rims and

\* This note is based on some routine studies of malaria investigations, a project under the auspices and with the support of the International Health Division of the Rockefeller Foundation co-operating with the Health Department of Madras Presidency and the Pasteur Institute of Southern India, in Coonoor, Nilgiris.

† Egg albumin is not mentioned in the original article but was suggested to us verbally by Dr. Rice as having been found useful. We agree that it is.

#### (Continued from previous column)

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supplied with corks—were each filled with 25 c.cm. of the stock suspension, the bottle being vigorously shaken at each pouring. These filled vials were then ready for use in the field, to which the spraying coolie took the following equipment (*see figure*) :



Fig. 1.—Coolie equipped to spray Paris green by dustless method. Carrying Hudson sprayer, tin dipper and funnel, 'cartridge' belt of vials containing stock suspension. Photograph also shows type of canal edge successfully treated by this method.

#### Field equipment

20 to 25 filled vials.

One khaki belt 4 to 6 inches wide (cartridge belt type). This was made with khaki drill by a tailor, and had individual pouches to hold vials.

One tin can measuring out exactly 1,000 c.cm. When not in use this was hung on a hook or a flap of the belt on the left side.

One tin funnel fitted with a wire gauze sieve.

One Hudson Sterling no. 115 sprayer.

The spraying coolie, with the above field equipment, proceeded to the breeding places and carried on as follows :—

#### Field procedure

1. Removed the pump from the sprayer.

2. Took 2 litres of water from the breeding place and poured it into the sprayer tank, filtering it through the funnel to remove any floating matter.

3. Removed one vial from his belt, vigorously shaking it and then pouring the contents into the sprayer tank. Taking a small quantity of

water into the empty vial, it was again shaken and poured into the tank to remove the last of the Paris green.

4. Poured three more litres of water from the breeding place into the sprayer tank as before. (This brought the total water used to 5 litres for every 25 c.cm. of stock suspension.)

5. Replaced the pump plunger and pumped to desired pressure.

6. Then slung the sprayer on his back and proceeded to spray, ordinarily keeping the nozzle 1 to 1½ feet above the water surface.

The sprayer tank was kept agitated now and then with a few swings of the hip. Ordinarily 700 to 900 square feet were sprayed with 25 c.cm. of stock suspension and an average South Indian workman used between 20 to 25 vials a day.

#### Use in Senjayakollai

This method was used in Senjayakollai as one phase of a control programme by minor engineering methods in that village. First season's spraying began on 15th July and ended on 5th December, 1938. The interval between treatment was 4 to 5 days from July to 5th November and thereafter 7 days. The unusually short interval allowed at first was due to the observation that *Anopheles culicifacies* larvae were developing at the rapid rate of one stage per day. The following breeding places were treated :

	Length (yards)	Area sprayed (square yards)
Branch irrigation canals ..	2,350	1,330
Irrigation channels ..	5,195	1,730
Tank edges ..	..	660
Borrow pits ..	..	2,500
Wells (120 sprayed) ..	..	94
Total area sprayed per time	..	6,814 (approx)

There were 33 spraying rounds during the period and our record of the number of vials used was 1,818 for 31 rounds, or an average of 58.6 vials per round. This means that approximately 107.7 square yards or 969.3 square feet were covered per vial. (We estimate that the width of sprayed area along a canal bank was 1 foot.)

During 1939, spraying by this method was carried out from 7th August to 25th December at intervals varying, as in 1938, from 4 to 7 days. In 1939 only field channels and ditches were sprayed. (In neither year were the extensive rice fields around this town treated.) The total length sprayed per round in 1939 was 5,305 yards and area sprayed was estimated at 1,768 square yards. There were 32 rounds of spraying in which a total of 629 vials was used. The approximate average area sprayed per vial in 1939 was 76.8 square yards or 691.2 square feet, somewhat less than in 1938.

### Discussion

As to quantity of stock suspension required, this will of course vary with types of place being sprayed. From some special field trials, we believe it is probably safe to say that an average of 500 square feet can be covered per vial in general use. This is about 60 square feet per cubic centimetre of Paris green. Our figures were higher, but we were usually dealing with canal edges. We frequently check our results, since all our work is on an experimental basis, and we are certain that this measure was effectively controlling breeding in the places sprayed, frequently even in the presence of considerable vegetation.

Several tests of the method were made, with careful larva counting before and after. In every case the test showed excellent results. One such test may be mentioned as an example. On 7th April, 1940, in a newly-made roadside drain, 85 feet  $\times$  3 $\frac{1}{2}$  feet, there were 12.7 anopheline larvæ, all stages, per standard dip. One pupa was found in the course of the dipping. Vegetation was scanty. This ditch was sprayed by the above technique in the usual way. Twenty-four hours later the ditch was again sampled by standard dipping but not a single larva was taken. One pupa was found and some freshly-laid ova. In an adjoining ditch, where no spraying was done, numbers of larvæ per standard dip were the same before and after the experiment. These results agree with other tests at other seasons and in other types of breeding places.

### Costs

Average expenses may be figured as follows for one day's spraying by our coolie of approximately 12,000 square feet, using 24 vials of stock suspension.

#### Recurring expenses

	Rupees*
Kerosene 500 c.c. at Re. 0-11-6 per gallon ..	0-1-3
Paris green 250 c.c. at Rs. 70 per 100 lb. ..	0-8-10
Egg albumin 1 gramme at Rs. 42 per 10 lb. ..	0-1-3
Cost of 750 c.c. stock suspension ..	0-11-4
Coolie, 1 day at Rs. 9 per month ..	0-4-9
Cost of 1 day's spraying ..	1-0-1

#### Initial expenses

	Rupees*
Hudson Sterling sprayer (115) ..	30-0-0
Spare parts .. ..	2-0-0
Vials .. .. (approx.)	8-0-0
Belt .. ..	2-0-0
Funnel, tins, etc. .. ..	3-0-0
Total cost for equipment ..	45-0-0

\* A rupee at present rate of exchange may be taken as equivalent to £0-1-6 or U. S. \$0.32. One rupee contains 16 annas and each anna 12 pies. Prices have risen due to war conditions. These are pre-war actual figures.

Footnote.—Some useful figures:—

- 100 c.c. Paris green weigh 142 grams or 0.313 lb.
- 100 c.c. Egg albumin (powdered) weigh 53 grams.
- 1 Imp. gallon kerosene oil = 4,564 c.c. equivalent to 1,2009 U. S. gals.
- 1 pound (avoirdupois) equals 454 grams.

Equipment should be good for at least two years, and the sprayer for considerably longer period if properly used. One might reasonably add As. 2 per day for depreciation and say that (at pre-war prices) one can treat effectively 12,000 square feet by this method per day using one coolie at a total cost of Re. 1-2-1 per time.

### Summary

Using a modification of the dustless method of diluting and spreading Paris green recommended by Barber *et al.* (*loc. cit.*), we have had excellent results, especially in treating irrigation canal and channel banks, during two seasons in south-eastern India. It is our belief that the method is effective, cheap, and simple.

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## A Mirror of Hospital Practice

### BANTI'S DISEASE?

By PRAN NATH CHHUTTANI, M.B., B.S. (Punjab),  
D.T.M. (Cal.)

*The 'Shalimar', Gangtok (Sikkim)*

In view of the case report of Banti's disease by Captain J. W. D. Goodall, I.M.S., in *I.M.G.*, July 1940, it may be of interest to record the following case:—

A Pathan farmer, aged 35, coming from Ghazni (Afghanistan), sought admission to the Mayo Hospital, Lahore, on 22nd December, 1938, to have his enlarged spleen removed.

*History.*—Twelve years before admission patient had noticed a mass under the left costal margin which he soon came to learn was his spleen. It had been steadily increasing in size all these years. Though for the first three or four years after this incidental discovery he was quite fit and without any other symptoms yet after this period he insidiously started feeling below the mark and would get attacks of epistaxis occasionally, to start with in the hot summer months only. The severity of these attacks was variable, the amount of blood lost being from a teaspoonful to about a cupful. At the same time he began to have attacks of intermittent fever which lasted for about a fortnight at a time and recurred every four or five months. Epistaxis and fever as above had been with him for about eight years before admission. He never had hæmatemesis or any other hæmorrhages. As the indigenous treatment did not benefit him and as he now also got breathless at work he left his country to have his enlarged spleen removed.

Family history revealed nothing relevant.

*Physical examination.*—General examination revealed anæmia; tongue and nails pale; no icterus; nothing abnormal in the circulatory and respiratory systems; spleen enlarged below the umbilicus. Consistency hard. In the middle of the palpable portion of the anterior border of the spleen there was a vague swelling about the size of an orange. Liver not palpable. No signs of ascites. No œdema.

*Laboratory investigation.*—Normocytic hypochromic anemia. There was eosinophilia of 12 per cent but no cause could be discovered. Stools showed no helminthic or protozoal infection. Wassermann reaction was negative. Preliminary and subsequent blood reports

*Acknowledgment.*—I wish to thank Lieut.-Colonel A. Chand, I.M.S., visiting physician and Professor of Medicine, Mayo Hospital and Medical College, Lahore, for so kindly permitting

TABLE

	DATE			
	14th January, 1939	2nd March, 1939	15th March, 1939	15th April, 1939
Hæmoglobin (Tallqvist method)	65 per cent	..	70 per cent	80 per cent
White blood cells per c.mm.	8,125	16,000	11,375	8,750
Red blood cells per c.mm.	3,560,000	..	2,850,000	3,960,000
Polymorphonuclears	54 per cent	73 per cent	70 per cent	34 per cent
Lymphocytes	32 " "	6 " "	14 " "	42 " "
Large mononuclears	2 " "	3 " "	0	0
Eosinophils	12 " "	18 " "	16 per cent	24 per cent
Size (Eve's halometer)	7.3 $\mu$	..	8.2 $\mu$	7.8 $\mu$
Bleeding time	2 minutes	..	1 minute 30 seconds	..
Coagulation time	4 minutes 45 seconds	..	4 minutes 15 seconds	..
van den Bergh reaction	Negative in all phases	..	Indirect only ++	..
Platelet count	Did not contra-indicate splenectomy, exact count misplaced.	..	160,000 per c.mm.	..
Reticulocyte count	..	..	3 per cent	2 per cent

have been tabulated. Urine was normal except for presence of urobilin.

Patient was sent back to the surgical ward with the visiting physician's opinion that though there was no indication for splenectomy yet there was no contra-indication for the operation. The patient was put on iron and ammonium citrate—90 grains a day—on 15th January, 1939, and ultimately, on 21st February, successful splenectomy was performed. There were no adhesions around the spleen and removal was easy. There was about a pint of effusion in the peritoneal cavity. Liver was markedly shrunken. It was the agreed opinion of everybody that its size was not more than one-eighth of normal. It had the characteristic hobnailed appearance. Recovery after the operation was interrupted by the development of broncho-pneumonia. Operation wound healed normally. He was referred back to the medical ward on 14th March when his respiratory complication had considerably improved. His blood report on 15th March showed macrocytic hyperchromic anemia (see table). van den Bergh—indirect was ++. Conjunctivæ bore obvious icterus. Patient was put on intensive campolon therapy and subsequently his blood picture and general condition much improved and he was discharged on 17th April, 1939.

*Point of interest.*—Advanced hepatic cirrhosis as seen on the operating table was surprising in view of absence of any definite clinical indication.

*Discussion.*—1. Can such a case be labelled Banti's disease? There was no leucopenia. There was history of repeated intermittent fever but it started after obvious enlargement of spleen had been there for four years. There was no definite evidence of malaria either—no malarial parasites could be found. (Patient did not have any fever during his stay in the hospital except that due to the post-operative complication of broncho-pneumonia.) Personally I feel a diagnosis of Banti's disease is justified.

2. Was splenectomy justifiable? In view of the advanced cirrhosis this seems questionable.

me to report this case of his which I had the chance to study when working as a house physician of his medical unit.

### SEVERE HÆMATURIA RESULTING FROM THE USE OF M.&B. 693

By KRISHNA GOPAL KARMAKAR, L.M.F.  
Resident Medical Officer, Carron Tea Estate, Carron P. O., Jalpaiguri

A FEMALE child, aged 6 years, was attacked with slight fever on the 2nd July, 1940. Her temperature came down to normal next day. But it rose to 102.5°F. at night and came down to 99°F. on the following day (4th July). Malignant tertian malaria parasites were found in the blood and 6 grains of quinine bishydrochloride were injected intramuscularly. Another injection of quinine was given in the same strength on the 5th July. But in spite of these injections the temperature was oscillating between 100°F. and 102.5°F. On the 7th and 8th July two more injections of quinine, 6 grains each, were administered. The fever did not yield. Bowels were constipated and moved by calomel and salts in the early stage. Later on, the child had occasional loose foul-smelling motions. Urine was very scanty during 24 hours. Pulse rate varied between 108 and 120 per minute. No abnormality was found in the lungs.

*Urine.*—Reaction—acid. Chemical examination—phosphates present. Microscopical examination—pus cells, epithelial cells, organisms—Gram-negative bacilli (*B. coli*?), diphtheroids, Gram-positive cocci in pairs and chains.

*Stool.*—No evidence of dysentery or helminth infection.

*Progress.*—The fever was irregular (99° to 102°F. axillary temperature). Hexamine was tried for three consecutive days from 11th to 13th July, to disinfect the urine, but it did no good. Four tablets of M.&B. 693 were given daily from the 17th to the 19th July. After three days of sulphapyridine treatment the child passed about 4 ounces of dark blood during micturition at 5 a.m. on 20th July. The specimen was sent to the laboratory and the report showed this to be hæmaturia and not hæmoglobinuria. The hæmaturia was thought to be due to the



toxic action of M.&B. 693 which was stopped immediately. Plenty of fluids and big doses of alkaline mixture were given. The child had intense pain in her lower abdomen and 5 hours later she again passed about 6 ounces of red-coloured urine. Tincture hyoscyamus was administered with alkaline mixture to relieve the spasmodic pain. Next time, she passed clear urine during defæcation. The hæmaturia took place on the 18th day of illness when the child was very devitalized owing to prolonged illness.

Another specimen of urine was sent to the laboratory for examination on the 21st July. Reaction—slightly acid, albumin—nil. Microscopical examination—red cells numerous, pus cells, epithelial cells—present, organisms—scanty, *B. coli*—present, few.

Lastly, the patient was given *B. coli* vaccine (P. D. & Co.) with steady improvement, the temperature gradually coming down to normal on the 6th August, 1940.

The case is of interest on account of hæmaturia apparently caused by the toxic action of M.&B. 693.

My thanks are due to Dr. Baird, the group medical officer, for his kind and valuable help in the treatment and to Dr. S. K. Sen, in charge of the Nagrakata Central Laboratory, for the pathological reports.

## A CASE OF AIR EMBOLISM AS A RESULT OF ARTIFICIAL PNEUMOTHORAX TREATMENT

By AMIR CHAND, F.R.C.P. (Edin.)

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Air embolism is a very rare but a very serious complication of artificial pneumothorax treatment. It occurs most frequently during the induction of pneumothorax, though cases have been recorded in which it occurred during a refill by the needle entering and tearing an adhesion. There are four possible methods by which air may enter the blood stream and cause embolism :—

(1) Air may be injected into a pulmonary vein owing to faulty technique.

(2) Air may be sucked into a pulmonary vein from the tubes and the manometer, there being negative pressure in these venous channels.

(3) The production of an air pocket under pressure may tear a recent adhesion and open up a venous channel in it, which may absorb the injected air. In such a case embolism may occur some time after the induction.

(4) If the needle should penetrate an adherent lung, the movement of the lung, with respiration, across the needle point might cause the needle to open a venous channel to the air of an alveolus or a bronchiole, from which, if it keeps open long enough, it may absorb large quantities of air.

Air embolism, though the most dangerous complication of artificial pneumothorax treatment (AP), is so rare, that we suggest the advisability of different workers recording the details of all cases of air embolism so that it may be possible ultimately to establish which of the above is the commonest cause. Only a proper comprehension of the causes will lead to the devising of proper methods to check this serious complication. The following case, which clearly illustrates what the cause was in this particular patient, is being published with this intention. This is the first case that we have had during the last four years during which period some thousands of AP fills, including some hundreds of primary fills, were given :—

A female, about 40 years of age, was admitted into the tuberculosis wards as a case of pulmonary tuberculosis. Artificial pneumothorax had been started on her left side at some other centre. An x-ray skiagram of the chest however revealed that the disease was bilateral, involving the whole of the upper lobe on the left side, and showing many foci of infiltration in the right upper and middle lobes.

It was decided to keep a selective collapse on the left side but also start a collapse by AP on the right side, and then maintain a bilateral selective collapse. However, before this could be done, she developed a small quantity of pleural effusion on the right side, and a high temperature as a result. After the acute stage passed off, it was decided to withdraw the effusion and replace it by air. Only a few ounces of clear fluid could be removed, but a needle passed a few interspaces above, showed the pleural cavity to be adherent there and no air was given. Next morning an attempt at AP was made again. After properly anesthetizing the tissues by 1 per cent novocaine, the pneumothorax needle was passed. The manometer failed to show any movement, and we were going to take out the needle, when the patient began to shout and cry aloud that something serious had happened. The needle was at once taken out. No air had been given because there had been no movement of the manometer. The patient continued crying aloud, and complaining of tingling and numbness all over the body, but more on the right side. She expectorated about one ounce of bright red frothy blood immediately after the needle was taken out.

As the patient was known to be very hysterical, it was at first thought that she had developed a hysterical fit. She however soon became semi-conscious, could not recognize anybody, and tossed about continuously in her bed. An examination of the nervous system revealed an exaggeration of deep reflexes all over the body, a positive extensor plantar response on the left side, and loss of abdominal jerks on the left side. It became clear by now that air embolism had occurred involving probably the cortical area on the right side. Examination of the heart revealed no abnormality in the sounds.

She gradually became completely comatose and began to show signs of complete hemiplegia on the left side. The face was drawn to the right side, both the pupils were dilated; the left was wider and completely inactive to light reflex and while she showed occasional automatic movements of the right side, the left side was completely immobile and flaccid.

This state of affairs lasted for many hours. The next morning she was found to be slightly better. The pupils were less dilated and both were reacting to light. She was partially conscious. The left side was still paralysed, but no longer flaccid. The knee and the ankle jerks on this side were exaggerated and the plantar response was extensor. She however soon became restless and violent, tossed about in her bed, was delirious and talked incoherently all the time. The physical signs remained unchanged. This state lasted



for three days. During this period there was complete insomnia and the ordinary hypnotics failed to give any relief. On the third night, the house physician on night duty gave her a dose of chloral hydrate at about 9 p.m. and 3ii of paraldehyde per rectum at midnight. As both these failed, he gave 1/6th gr. of morphin at 4 a.m. She went to sleep at about 12 noon, continued sleeping till about 4 a.m. next morning and woke up quite calm, and in her senses. The paralysis began to pass off gradually and had almost completely disappeared in another four or five days.

The case is obviously one of air embolism—probably involving the cortical area on the right side, though exact localization was not possible, as so long as the delirious state lasted complete examination of the nervous system could not be done. This case, however, presents certain peculiar features. No air was given and hæmoptysis occurred at the start of the symptoms. It may be argued that there might have been some sucking of the air from the tubes and the manometer by some pulmonary vein. In that case there should have been some movement of the manometer, but there was none. Hæmoptysis however gives the clue. It seems that the needle passed into the lung substance, ruptured some pulmonary vein, and the open vein, owing to the negative pressure in it, absorbed large amounts of air from the ruptured lung alveoli or bronchioles. Many workers have put forward the view that this is the predominant if not the sole cause of air embolism in artificial pneumothorax cases. This case proves that this is certainly one of the causes. This fact is, in our opinion, of practical significance in one important aspect. If this view of air embolism be accepted, we should use even for primary fills thin needles rather than the usual thick blunt needles, so that the tear in the vein when it does occur may not keep open. Moreover, there would be no use employing special gases like oxygen or carbon dioxide for the primary fills as is the practice in some centres.

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#### A CASE OF ABDOMINAL PREGNANCY

By (Mrs.) S. MOZUMDAR, M.B. (Cal.), F.R.C.S. (Eng.)  
Superintendent, Zenana Hospital, Jammu,  
Kashmir State

A PATIENT was admitted into the hospital on 6th April, 1940, for an abdominal tumour. The history was that about 13 months ago she thought she became pregnant and had all the signs and symptoms of pregnancy to the end of full nine months. She seemed absolutely certain on the point of foetal movements, but not much faith was put on her statements, as so often the observations of these village women are inaccurate and therefore misleading. At the end of nine months, when nothing happened, she went to a hakim who gave her some 'strong' medicine and her abdomen started shrinking. From the size of a full-term pregnancy, the tumour had reduced to that of

about seven months. But finding that it did not reduce any further, she sought the aid of the hospital.

**Examination.**—The patient was of an average build, middle-aged, had six children, was slightly anæmic, and debilitated. There was a hard, painless, lobulated tumour in the abdomen, rising well above the umbilicus; a much larger lobe on the right side, separated by a groove from a smaller lump on the left. The mobility was fair but not too free. There was no thrill and no sign of inflammatory trouble. The tumour was taken to be a uterine fibroid, with a possible left parovarian cyst added on (the left lump was in fact a parovarian mass, as it turned out on operation). The patient having agreed to a laparotomy, I opened the abdomen under spinal anaesthesia on 18th April. Directly on opening the peritoneal cavity, I found some dark reddish-green fluid in the abdomen, and a fully-formed full-term foetus lying free in the abdomen. The larger right lobe of the tumour was the curled up and twisted foetus, and the left lump was the rolled up, smoothed-out placenta, implanted on the original site of ruptured left fallopian tube. The fimbriated end of this tube was clearly seen while examining the specimen after the operation, so that it was not a case of tubal abortion—but one of tubal rupture, as the placental mass was implanted about midway down the length of the left tube. The ovary also was intact on this side; the whole foetus, with cord and, this implanted placenta, was removed *en bloc* by resection of the left tube near the uterine end. Fortunately, in this case, the placental implantation was on a small compact smooth surface—and was not adherent to any other organ in the abdomen, which is so often the case, leading to severe hæmorrhage on trying to remove the placenta.

The patient made an uneventful recovery.

The interesting part of the case is the very correct and accurate history given by the patient, which was not taken seriously by us as so often their histories are misleading, specially with regard to pregnancy and foetal movements.

During convalescence, the patient was questioned again regarding the pain, etc., during the time of the tubal rupture—but it was all negative. Evidently, here was a case of very gradual stretching of the tube and escape of the foetus into the abdomen in a 'genteel' manner, without any of the violent symptoms of an acute abdomen.

The patient left the hospital on the 26th day.

#### A CASE OF SELF-OPERATION FOR VENTRAL HERNIA

By M. M. D. CHUGHITAI, M.B., B.S., M.R.C.S., L.R.C.P.,  
L.M., D.T.M. & H., D.P.H., D.O.M.S.

Divisional Medical Officer, North-Western Railway,  
Quetta

A PATIENT, Anglo-Indian male, apparently intelligent, aged about 48 years, a railway shed man, was brought to hospital for admission on 6th June, 1940.

**History.**—The patient had had a ventral hernia about the size of a big orange for the past six years. On 2nd June, 1940, he cut the protruding part with a sharp pair of scissors, sutured the skin with an ordinary needle and thread, and carried on his usual routine of life. He stated that he sterilized the instruments by boiling and washing his hands. On the morning of 6th June, presuming that the wound had healed, he took out the stitches. Soon after, he had a fit of coughing and the wound gave way. A part of the intestines gushed out but he kept them back with the pressure of his hands.

**Condition on examination.**—There was a transverse wound about 4 inches in length through all the layers including the parietal peritoneum at the level of the umbilicus and nearly half of the small intestines was protruding out of the abdomen. General condition of the patient, however, was fairly satisfactory. The gut remained exposed for about 15 minutes.

*Treatment.*—The patient was immediately anesthetized and the gut pushed back into the abdomen with great difficulty. The peritoneal cavity was closed. The two recti were approximated and sutured, and the abdominal wall closed. Drainage was maintained through a small tube which was removed after 48 hours. The patient developed slight temperature which was suspected to be due to sepsis and was accordingly treated with Baeteramide injections.

The patient was discharged after three weeks and is doing his usual duties with a protective bandage.

I am indebted to Dr. S. C. Chatterjee, Chief Medical and Health Officer, North-Western Railway, Lahore, for giving me valuable suggestions and permission to publish these notes.

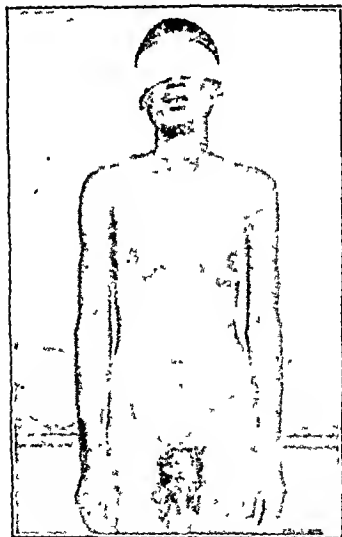
## DEVELOPMENT OF SOME FEMALE SECONDARY SEX CHARACTERS IN AN ADULT MALE

By P. N. GHOSE, M.B.

Medical Officer, Kanknarrah Jute Mills, Kankinara

Mr. X, Hindu, male, aged 24 years, married at 18 years and had got a male child of 2½ years age. He says at 21 years of age, i.e., about three years ago, his breasts started to develop, and at present they are fairly big in size. The lumps inside get periodically swollen and become painful, but there is no secretion up till now. He says since his breasts started developing his voice is becoming sharper, and his penis and testicles are getting smaller. His sexual desire is intact all along.

On examination Mr. X looks a thin-built young man, with a narrow chest and a rather broad pubis,



with scanty development of hair on his face. His voice is rather sharp and more like a female than an adult male. His breasts are fairly big in size. The left one is bigger than the right. There are dark pigmented areola with thick pigmented nipples. On palpation there are definite glands with ducts and they are tender on pressure.

The external genitals are those of an adult male type. The two testicles with cords are there. The penis and the testicles are rather smaller than the average size. There is no

abnormal opening anywhere around the perineum.

The case is under observation for further development.

## AN UNUSUAL CASE OF ANAPHYLAXIS

By R. M. LLOYD STILL

MAJOR, I.M.S.

Civil Surgeon, Myitkyina, Rangoon

and

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On 25th November, 1939, one Dr. A received an injection of anti-tetanic serum 500 units, for a

shoe-nail bite on his heel. Almost at once he developed the following symptoms and signs:—

(1) *Symptoms.*—Severe constricting pain across the chest, inability to breathe properly and giddiness.

(2) *Signs.*—Cyanosis of the face, urticarial eruptions all over the body and weak pulse leading to a complete collapse.

Realizing that he was having an attack of severe serum sickness, adrenalin 1/1,000 1 c.cm. was given subcutaneously and artificial respiration was carried out for a short time. He recovered from the acute symptoms within half an hour but felt very weak and giddy. This feeling of constriction across the chest continued throughout the day but with diminished severity. He was given calcium lactate gr. x, three times a day. He passed a restless night.

On 26th November he complained of distension of his upper abdomen with feeling of nausea and belching. He gave himself a double dose of Seidlitz powder to relieve his distension. During the course of the day he did not pass a motion or any flatus and there was no relief of his abdominal distension. A turpentine enema was given with no result. By the evening the distension was accompanied with severe colicky pain in the upper abdomen. Pituitrin 0.5 c.cm. gave him no relief and morphia ¼ gr. with atropine was given to relieve him and induce sleep.

On 27th November he was transferred to the civil hospital, Myitkyina.

He was a well-nourished man of 28 years.

*Past history.*—(a) Two years ago when he had received an injection of anti-tetanic serum, he had an attack of urticaria which had yielded to treatment with adrenalin.

(b) History of amoebic dysentery when he was a student. During that time had had a full course of emetine.

A complete physical examination was done on admission and the findings were as follows:—

Pulse—104 per minute, temperature—100°F., respiration—26 per minute. No anæmia, no jaundice, no enlargement of glands. Tongue—coated, furred but moist. Gum and teeth—normal. Abdomen: Inspection—moderate distension of upper abdomen. Moves freely with respiration. Palpation—no definite rigidity was present anywhere but tenderness and guarding of the muscles on deep pressure were discovered in both the hypochondriac areas. There was no localization of tenderness.

Liver and spleen were not palpable.

Percussion—tympanitic resonance found all over abdomen. Auscultation—intestinal gurgling noises could be heard in all the four areas of the abdomen. Heart and lungs—nothing abnormal detected. Jerks and superficial reflexes were normal. Rectal examination showed no tenderness in the appendicular area.

The following treatments were given:—

(1) Pituitrin 0.5 c.cm. was injected and half an hour after a flatus tube was passed. There was no result. A turpentine enema was given with return of clear fluid and no result.

(2) He was placed in Fowler's position and turpentine stupes were given four hourly.

The pulse rate, temperature and the rate of respiration were recorded hourly.

The following examinations were done that day:—

(1) Blood for malaria parasites, with negative result.  
(2) Blood for total and differential counts with the result: Polymorphonuclears—87 per cent, lymphocytes—8 per cent, large mononuclears—4 per cent, eosinophils—1 per cent, basophils—nil.

Total white blood corpuscles—12,000 per c.mm.

In the afternoon the distension was causing him intense discomfort and pain and he became very restless. The pulse went up to 118 per minute, respiration 28 and temperature 101°F. A stomach wash with sodi bicarbonate a drachm to a pint was given with immediate relief. It may be mentioned here that from the 25th the patient had taken nothing by mouth and therefore rectal saline with glucose was given every four hours since admission.

The relief after the stomach wash was only temporary because by 8 p.m. in the evening he again complained of distension. The distension again became most distressing and in the early hours of the 28th he begged to be given a stomach wash to relieve him.

Our diagnosis was one of either acute cholecystitis or acute pancreatitis, and surgical interference was considered but did not appear justified. We decided to call a surgeon in consultation. He agreed that a laparotomy was not justifiable.

On the 28th the stools were examined and found to contain Charcot-Leyden crystals. A course of emetine was commenced. Urine was examined and nothing abnormal was detected except a trace of albumin.

The temperature on the 28th morning was 99.4°F., pulse 102, respiration 24. During the course of the day, temperature and pulse remained steady. The day passed in a similar manner, i.e., severe distension of the upper abdomen, relieved temporarily by stomach wash and this was done three times during the day.

A carminative mixture was given three times a day and pituitrin 0.5 c.cm. twice daily. Calcium gluconate 10 per cent was injected intramuscularly once only. He took a little ovaltine and a few sips of beef tea. Paraldehyde was given at night to induce sleep but with no effect.

On the 29th his condition was similar except that tenderness of the abdomen was localized to the gall-bladder area, but Murphy's sign was not positive. He still complained of a colicky pain starting from the right hypochondriac region and passing across the upper abdomen ending somewhere near the splenic area. The temperature went up to 102°F., pulse to 120 per minute and he showed signs of exhaustion. Urotropine grs. 10 was added to the mixture. Bismuth salicylate was given in  $\frac{1}{2}$  drachm dose three times a day and ephedrine sulph. was given in  $\frac{1}{2}$  gr. dose. Nothing gave him any real relief except the stomach wash. This too was for only a few hours giving way to severe distension, agonizing pain and restlessness.

On the 30th certain signs appeared which supported our diagnosis of acute cholecystitis, e.g., icteric tinge of conjunctiva, presence of bile in the urine and definite tenderness in the gall-bladder area, where a lump was felt. Morning temperature came down to 99°F. and maximum during the day rose to 102°F. Pulse was between 104 and 120 per minute. We then gave fractional doses of calomel and olive oil an ounce at night.

But till the early morning of 1st December stomach wash had to be carried on as frequently as before and he craved for it.

On the 1st December his condition showed signs of definite improvement. The colic had disappeared and no stomach wash was required. Although the distension was still present it was no longer causing him much discomfort. The icteric tinge of the eye became more pronounced. He was put on the following diet:—

Coffee, barley-sugar, glucose water, Bovril, chicken broth and a small quantity of Benger's food. The maximum temperature was 101.4°F. He passed a lot of flatus and also had a few motions without enema.

From the 2nd December the condition progressed rapidly towards recovery and he was treated mainly as acute cholecystitis.

### Comments

The case has been described in detail as this is the first of its kind encountered by the writers and no mention could be found in any textbook.

In the *Indian Medical Gazette* of November 1939, mention has been made of serum sensitivity in families, but no such family history is forthcoming in this case.

The patient is now well and at work but states that he is unable to take any fatty food.

The final diagnosis of acute cholecystitis was of course not difficult. The problem concerns

the aetiology and pathology. Our suggestion is that there was an allergic condition causing swelling and hyperæmia of the whole intestinal tract which eventually settled in the gall bladder giving rise to the signs and symptoms mentioned.

### A CASE OF DUODENAL OBSTRUCTION

By RICHARD E. STRAIN, M.C.P.&S., M.C.C., M.D.

*Miraj Medical Centre, Miraj, India*

A WOMAN, 35 years old, was admitted to the Miraj Medical Centre complaining of sudden onset of severe pain in the right lumbar region eleven days previously; onset was noted at 4 p.m., after a big meal and while the patient was urinating. Pain was localized and so severe that the patient was carried home immediately and remained in bed until admission into the hospital. At 10 p.m. vomiting was first noted; vomitus was bile-coloured and contained only food particles. Vomiting had persisted until admission—no hæmatemesis noted. Vomiting was promptly initiated by taking food or fluids by mouth and was associated with cramping pain in the epigastrium preceded by visible, palpable, and audible peristalsis. Several bowel movements without mæna occurred after onset, the patient having had a bowel movement the day of admission described as small and hard. Dysuria without hæmaturia and associated with nocturia (two to three times) had been present several months. No chills, fever, injury, or history of digestive distress was obtainable.

Physical examination disclosed a woman with dry skin and tongue. Temperature—97.6; pulse—116; respirations—20; blood pressure—116/70. Pyorrhœa was marked. Chest, heart and lungs were normal.

On inspection the abdomen disclosed a narrow sub-costal angle below which fleeting peristalsis was visible. After drinking two teaspoonfuls of water, this was immediately markedly exaggerated; the movement being from the left costal margin to the right. When the wave reached the right costal margin, gurgling was heard without the use of the stethoscope. No distension was noted. Palpation disclosed extreme rigidity of the right lumbar region extending anteriorly almost to the mid-line of the abdomen. Some spasm and rebound tenderness was noted in the right lower quadrant. A flat note to percussion was noted over the lateral portion of the right upper quadrant and down the lateral side of the right lower quadrant. No definite masses were palpable.

It was thought that the patient was suffering from a perforated ulcer (localized) with some spread down the para-colic gutter and associated with partial obstruction of the duodenum or a peri-renal collection causing obstruction—the exact nature of this being uncertain.

Laboratory examination disclosed: hæmoglobin—58 per cent (14.5 gm. as 100 per cent); red cells—4,710,000; leucocytes—26,400; differential count: polymorphonuclears—90 per cent of which 20 per cent were young non-segmented or 'stab' cells; 10 per cent lymphocytes. Catheterized urine—reaction alkaline; specific gravity—1.005; albumin—one plus (basis of one to four); sugar—negative; leucocytes—four plus; red cells—one plus.

Glucose intravenously and by proctodysis was given; duodenal intubation was started; a transfusion of 400 c.cm. of citrated blood was given. Mouth hygiene consisting of saline mouth washes alternating with Dobell's solution were started at once as a foul mouth was noted. A 'flat plate' x-ray of the abdomen disclosed only increased density in the right upper quadrant.

The following morning the right lower quadrant was quite rigid; a doughy irregular mass was palpable, thought to be matted intestines, over the pubic bone and into the right lower quadrant extending to the umbilicus. Blood urea was reported at 152 mg. per 100 c.cm.; Kahn test was negative. It was thought the process was spreading, possibly owing to increased tension and gangrene, so operation was decided upon. Because of the marked lumbar rigidity and to keep from contamination of the general peritoneal cavity, the incision was placed far laterally in the right upper quadrant.

Under local anaesthesia the peritoneal cavity was opened and normal small bowel displaced. The colon was not seen. No free fluid was present. On displacing the small bowel at the mid-line and apparently just below the greater curvature of the stomach there was a black, gangrenous mass about five inches in diameter with numerous soft spots felt. A hand could be inserted posteriorly part of the way round the mass but it seemed continuous with the vertebral column. As it seemed cystic, aspiration was attempted and 2 c.cm. of dark blood was obtained. The mass was incised and two handfuls of old blood removed. Nothing could be felt in the cavity except an irregular lining wall. A drain was inserted in the area it being thought the patient had had a pancreatic hæmorrhage or a ruptured posterior ulcer, although the pylorus felt normal as far as one could judge.

Post-operatively the patient responded well; the temperature reached a peak of 99.2°F. the first 24 hours and remained normal the second 24 hours. Blood urea was reported at 160 despite a fluid intake of over 3,500 c.cm. of glucose and saline daily with a urinary output of 1,200 c.cm. The third post-operative day the afternoon temperature rose to 102; slight swelling and pain was noted over the left parotid which increased rapidly and markedly. Lugol's solution was started, 20 minims every two hours, after the technique of Leithauser and Cantor (1940) who report 23 consecutive cases so treated without a death. Despite aspiration and Lugol's solution, the patient died five days after operation and three days after the onset of parotitis.

Permission was secured for abdominal post-mortem examination. The drain inserted in the mass was well walled off by omentum and small bowel. The remainder of the abdomen was clear. The cæcum was found in the left lower quadrant—the ascending colon going to the splenic flexure; turning back upon itself without obstruction to form the descending colon. The descending duodenum was greatly dilated measuring five inches in diameter. Just medial to the right kidney was a black mass which was retro-peritoneal and by pressure upon the duodenum (which was quite securely held retro-peritoneally rather far to the right of the mid-line) had produced obstruction. All the peri-renal tissue was quite hæmorrhagic; no pus was encountered; the capsule stripped easily from the kidney; there was no gross evidence of injury or damage to the kidney itself. The renal vessels were completely bound up in a mass of partially organized blood clot a little over four inches in diameter. It was impossible to trace the original course of the renal vessels but it appeared that the original hæmorrhage must have come from one of the renal vessels, as the mass so securely enclosed them and hæmorrhage faded as this area was moved away from. The aorta appeared normal.

The pancreas, liver, and spleen were normal in appearance. The duodenum, when incised, was normal except for the marked dilatation.

This presents an interesting case of duodenal obstruction associated with a congenital anomaly of the colon; the obstruction was caused by a retro-peritoneal hematoma whose origin seems to have been a spontaneous hæmorrhage from one of the renal vessels without gross evidence of injury to the kidney. Death probably was caused by the severe parotitis, as the patient's

abdomen was quite soft without distension and food in small quantities was being taken without discomfort before death.

#### REFERENCE

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### PER-RECTUM M.&B. 693 IN A CASE OF PNEUMONIA

By S. R. LOKRE, L.M.P.

*Private Practitioner, Residency Indore, Indore (C. I.)*

A boy aged seven years was suffering from high fever, rapid pulse, hurried respiration, cough with rusty sputum, and pain in the chest. Bacteriological examination of the sputum was not practicable but clinically the signs confirmed it to be a case of pneumonia in which the whole right lung was involved.

A mixture containing liquor ammonium acetatis, sodium citrate, sodium bicarbonate, aromatic spirits of ammonia, tincture digitalis, brandy, syrup tolu, and water was given four times a day. Along with this one tablet of M.&B. 693 suspended in a little water was ordered an hour after the dose but it was not retained. I tried it in milk, but the patient vomited it again. Next I tried M.&B. 693 with a nicotinic acid tablet and gave them as a paste in honey but the combination did not agree with the patient and he vomited.

Next day the patient became semiconscious and showed signs of meningism which induced me to give M.&B. 693 per rectum. I dissolved two tablets of M.&B. 693 in one ounce of milk and gave it per rectum morning and evening. They were retained. For three consecutive days I continued the process as he tolerated the drug well when given per rectum. Combined injections of transpulmin 1 c.cm., redoxon 1 c.cm. and cardiazol-ephedrin m. 5 orally were also given last thing at night.

On the fifth day with this line of treatment his temperature, respiration, and pulse settled and congestion of the lung cleared. Thereafter the patient made an uneventful recovery.

The case is reported so that others may be induced to use the rectal route when the patient is unconscious and oral administration causes vomiting.

### SUB-LINGUAL GLAND CALCULI

By KAMAL NAIN, L.T.M., I.M.D.

*Shahpur City*

A MOHAMMEDAN female aged about 45 years, thin, came to me with a sub-lingual swelling and pain. Its duration was 15 to 20 days. She had a feeling of discomfort and pain on touch and pressure.

*Examination.*—There was a swelling about half an inch from the lower surface of mouth on the inner side of the cheek towards the anterior part. It was semi-soft and had a feel like an abscess. I gave her some gargle and advised her to come the next day. She felt discomfort and pain and had the swelling opened at a hospital and felt better after the tension was relieved. After three days she again came to me and wanted me to examine her as she was still getting pain. I saw a white spot in the wound and seized it with forceps and a hard nodular stone about an inch long came out. I made a thorough search and found another of similar size. After that the wound quickly healed up.

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### CONTRAMINE

Contramine is used in the chronic stages of disease such as rheumatic conditions, gonococcal infections and in chronic metallic intoxications. Contramine is normally administered as a solution by intramuscular injection, but it is available also in pessaries for the treatment of gonorrhœa and leucorrhœa in women; Contramine suppositories and bougies are also available.

### THIO-HISTAMINE

Thio-histamine, which consists of histamine in combination with sulphur, is similar to Contramine in pharmacological and therapeutic effects but it is used in the treatment of acute cases of gonococcal and other bacterial infections.

*Stocks of B.D.H. Medical Products are held by the principal chemists, and full particulars are obtainable from:*

**THE BRITISH DRUG HOUSES LTD.**  
(Incorporated in England)

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BOMBAY



# Indian Medical Gazette

DECEMBER

## THREE QUARTERS OF A CENTURY OF UNINTERRUPTED PUBLICATION

THE present number completes our seventy-fifth volume.

The first number of the *Indian Medical Gazette*, dated January 1866, appeared in a very different world from the present one. In India, Her Majesty's Government had taken over the functions of the East India Company just eight years before, and the Suez canal was nearing completion, but was not officially opened until three years later, so that the early numbers of this journal had to be carried round the Cape before they could be read in England. It is tragic that the later numbers of our seventy-fifth volume should once more have to travel the same way—but for a very different reason.

### *Medical Science, 1866 to 1940*

The scientific world has undergone even greater changes since our first number saw the light of day. In 1866, Darwin's *Origin of Species* had been published only seven years, antiseptic surgery was still unknown, and Pasteur had just finished his famous *Études sur le vin*, was investigating the silkworm disease that was threatening the silk industry of France, and had not yet turned his attention to human disease. Cholera was raging in Europe, whither it had travelled overland via Egypt; the opening of the canal a few years later provided a more direct route for epidemics of this mysterious disease—mysterious in that its cause was not discovered until nearly 20 years later; subsequent epidemics took only a few months to reach Europe from their home in India, but international quarantine regulations, based on our knowledge of the cause of the disease, have changed this channel of infection into a veritable filter which protects Europe and western countries, not only from cholera but from many other epidemic diseases. The next year, 1867, Lister introduced antiseptic surgery and in this branch of medical science a new era began. An event which went largely unnoticed at the time, for its repercussions in tropical medicine could not be anticipated, occurred in 1874 when Ehrlich introduced the dried stained blood smear; six years later Laveran demonstrated the malarial parasite, but thirty-one volumes of the *Indian Medical Gazette* had been published before Ross discovered pigmented bodies (oöcysts) in two 'fawn coloured' mosquitoes (anopheles) in the small laboratory in the grounds of the Presidency General Hospital in Calcutta (September number, 1897). But meanwhile, other things had been happening; in 1873 Obermeier discovered

the spirillum of relapsing fever, in 1880, Eberth isolated the typhoid bacillus and Evans—an Anglo-Indian veterinarian—discovered the trypanosome of surra, in 1882, Koch, who six years earlier had cultivated anthrax in artificial medium, discovered the tubercle bacillus, and in the following year the cholera vibrio, and in the same year Klebs discovered the diphtheria bacillus. In 1887, Bruce discovered the causative organism of Malta fever, in 1894, Kitasato the plague bacillus, and in 1897 Shiga the bacillus of dysentery. During this period Manson was working out the cause and method of transmission of filariasis, and his inspiration and suggestions undoubtedly led up to Ross's great discovery. The next century opened with the discovery of the trypanosome as the cause of sleeping sickness, and leishmania as the cause of kala-azar and oriental sore, although an unmistakable Leishman-Donovan body had been depicted in an article in the *Indian Medical Gazette* of 1885 by Cunningham who described it as the probable causative agent of the latter disease, and in 1905 Schaudinn discovered the treponema of syphilis.

The first 40 years of the life of the *Indian Medical Gazette* constituted a great age of parasitological discovery; the subsequent period saw possibly even greater advances in a variety of directions. In 1910, chemotherapy was virtually born with Ehrlich's discovery of salvarsan as an anti-syphilitic remedy. Its early triumphs were mostly in tropical medicine; although Germany had lost her colonies, paradoxically her chemists enjoyed an almost complete monopoly and at the conclusion of the 1914-1918 war a flood of synthetic preparations was released from the big German chemical factories; amongst the most successful of these were Hans Schmidt's series of pentavalent antimonials used from 1918 onwards, with such dramatic results in the treatment of the hitherto fatal kala-azar, and Bayer 205 which though over-heralded has taken an important place in the treatment of human trypanosomiasis and a more important one in that of cattle. In 1926, plasmochin appeared and four years later atebirin, the first synthetic compound that could be used in the place of quinine in the treatment of malaria (the first published report of its clinical use appeared in the *Indian Medical Gazette*, April 1932); finally in 1935, the sulphanilamide group of preparations, which were led by Domagk's 'prontosil', brought this chemotherapeutic era to what one feels, must be its crescendo, though the crescendo is still being held. Even before the war, the British and American chemists seem at last to have begun to take the initiative, and during the last few years many of the most valuable preparations have been of British origin, so that we are not handicapped in 1940 as we were in 1914.

Two other branches of medical science, endocrinology and radiology, came into being, as

such, during the latter half of the journal's career, though foreshadowed in its earlier days, by the work of Claude Bernard (1813-1878) and Brown-Sequard (1817-1894) who formulated the theory of internal secretions, and in 1895 by Röntgen's discovery of x-rays. Both have made steady and at times dramatic advances throughout this period.

Finally, at the very beginning of the century, the vitamin theory was originated by Hopkins (1906) and given more definite form in 1912 by Funk. From the original three, A, B and C, the vitamins have multiplied like the traditional rabbit; vitamin D was identified in 1920, vitamin E in 1922, and since then the early vitamins have been divided and subdivided, and entirely independent ones have been added, so that they number far more than the 26 letters of the alphabet, even if the orderly labelling had been maintained. This discovery of the vitamins was not only in itself of the greatest importance, but it has had a most stimulating effect in our attitude towards that fundamental medical science, dietetics, which during the 'parasitological era' was tending to be neglected. Most of the early vitamins have been chemically identified and many have been synthesized, as also have many of the endocrines, so that if the first half of this journal's life was spent in a parasitological era, the second half must be called an era of chemistry.

#### *Early Contributors*

All these great advances and sweeping changes in medical science will be found reflected month by month in the *Indian Medical Gazette*, whilst in many instances the first announcement of an important discovery was made in its pages; in fact a very fair history of not only tropical, but modern medicine as a whole, could be written from a careful study of these seventy-five volumes. We have not made any such detailed study, but a perusal of the early volumes shows that most of India's famous medical scientists, and these have been not a few, have used the *Indian Medical Gazette* as their mouthpiece; these include such men as Vandyke Carter, Norman Chevers, Sir Joseph Fayrer and D. D. Cunningham, to mention some of the earlier ones, but the journal numbers amongst her contributors others besides those who had adopted India as their field; for example, in the number for February 1872 there is a letter from Charles Darwin commenting on a paper that had appeared a few months earlier. To Sir Ronald Ross's contributions we have already referred. Sir Leonard Rogers was an early and regular contributor. The original papers on all his important work on kala-azar, emetine in amœbic dysentery, and intravenous saline in cholera will be found here. The earliest contribution we have found was 'on the use of calcium chloride to lessen hæmorrhage during operation with an illustrative case' in the May number, 1896, and his last, on epidemic forecasts, in March 1933,

37 years later. Another famous medical scientist, also fortunately still living, who was a frequent contributor, is Sir Robert McCarri-son; his first paper appeared in April 1903.

#### *Medical Publications in India*

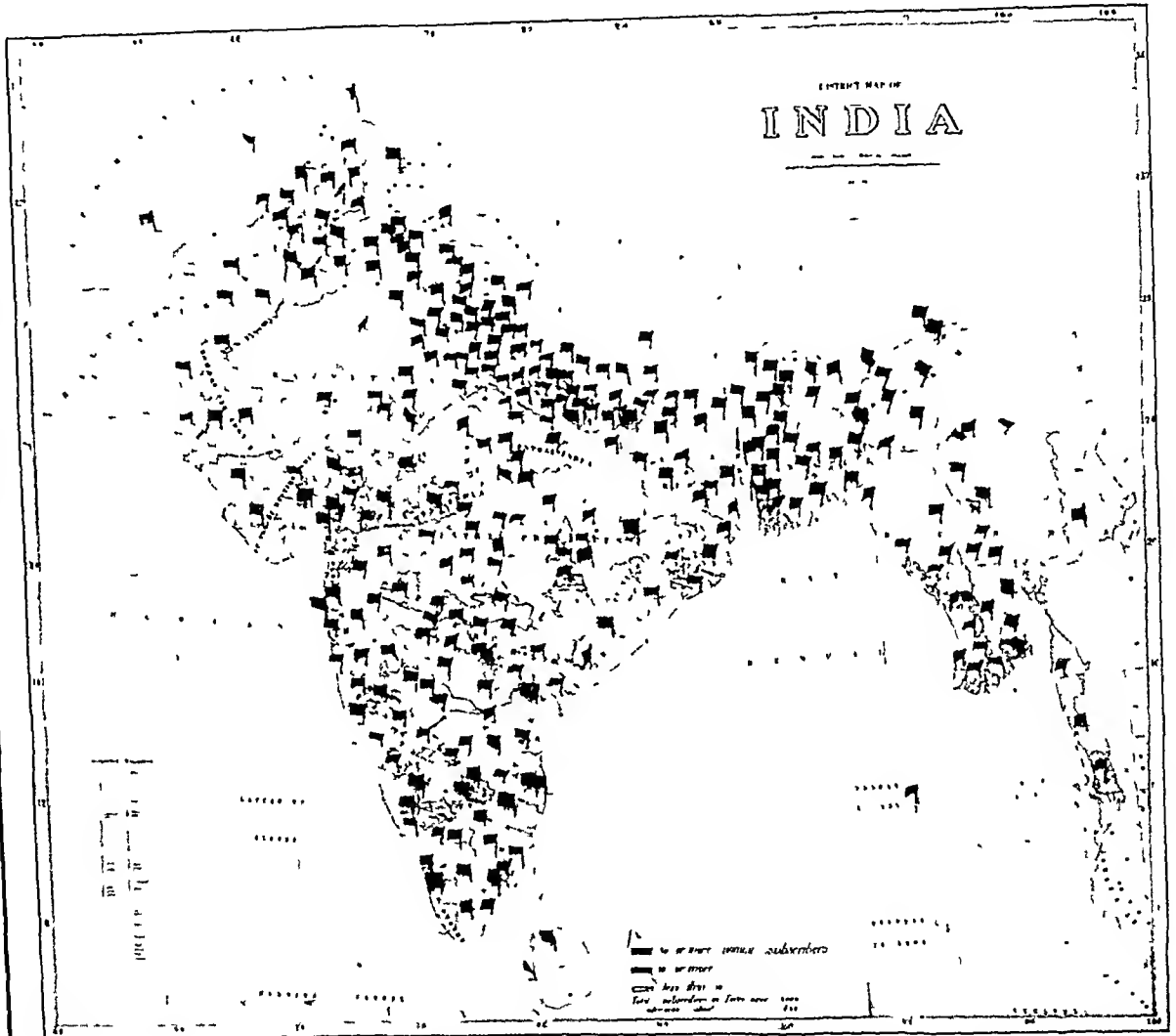
In 1866, medical publication in India was not in a very flourishing state, though it was by no means in its infancy, for in 1825 the *Transactions of the Medical and Physical Society of Calcutta* was published (by Messrs. Thacker & Co.) at first annually, then biennially, for a short time quarterly, and later irregularly, until 1845. The *Transactions* of a similarly-named Bombay society was first published in 1838 and maintained publication for at least 50 years; according to Crawford (*History of the Indian Medical Service*) it was still being published in 1914, but we can trace no volumes since 1889, and even up to that date it had obviously not appeared very regularly. Many other medical and scientific journals were published and enjoyed careers of various length, usually short; others were announced but did not appear. An exception appears to have been the *Indian Annals of Medical Science*, latterly published by Thacker, Spink & Co., which ran for 23 years from 1854 to 1877 and overlapped the *Indian Medical Gazette* by 11 years.

In its early days, the *Indian Medical Gazette* had no serious rivals and it can claim not only to be the oldest journal in India that has maintained monthly, or even regular, publications up to the present day, but to be the oldest such medical journal in the Eastern hemisphere. Crawford, in his book referred to above, said 'the *Gazette* has been the most successful and most important medical journal issued in India' and 'now after 47 years it shows every sign of a vigorous future career'. To-day, 28 years later, we believe that the same words could well be applied.

In more recent years many other medical journals have come into the field. In 1911, the *Indian Journal of Medical Research* was first published. This has never been in any sense a rival of the *Gazette*, but it did relieve the pressure on its space, by publishing many scientific papers which, though not entirely suitable for the general medical reader, naturally claimed the right to appear in India's leading journal.

The *Indian Medical Gazette* is an all-India publication and not in any sense local, not we sincerely believe in its outlook, in its contributors, nor in its circulation. Contributions come from all parts of India, as will be seen by a reference to recent numbers. An analysis of the 'original communications' during the current year, excluding the current number, shows that out of 153 contributions, only 65, or distinctly less than half, came from Bengal, 18 each from Bombay and Madras, 14 from the Punjab, 12 from Indian States, 8 from Assam, and 6 from the United Provinces; other British Indian provinces provided 8, Burma 2, Ceylon

# Distribution Map of INDIAN MEDICAL GAZETTE



Photograph of a map of India which shows the wide circulation of the Indian Medical Gazette. In the original map the flags are coloured, red indicating 50 subscribers and green 10, and numbered; this gives a more accurate idea of the relative number of subscribers in each district, but the figures are not visible in this photograph.



1, and Afghanistan 1. The circulation also is essentially all-India in character, as the accompanying map shows, though it has a quite considerable foreign circulation. Nevertheless, as Calcutta is thirteen hundred miles from Bombay and over a thousand from Madras, to mention two other important medical centres, it is not unnatural that medical men in these provinces should want to have their own journals. The *Antiseptic*, first published in 1904, in Madras, has had a successful career and is still appearing. In Bombay earlier ventures in the way of monthly journals have not been very successful, but seven years ago a fortnightly, the *Medical Bulletin*, appeared and is maintaining a high standard both from a literary and a scientific point of view. In Calcutta, the *Calcutta Medical Journal*, the journal of the Calcutta Medical Club, has had a successful career of 36 years, in its own sphere, as also has the *Journal of the Indian Medical Association*, first published in 1930 as the *Indian Medical World* and under its present name in 1931. An example of a specialist journal is the *Indian Journal of Pediatrics*, a carefully edited and well-printed journal, which has appeared quarterly since 1933, and as time goes on there will be room for many more specialist journals of this type, for the number of good-class contributions that are sent to us is far beyond the capacity of one journal and many have to be refused on grounds other than their scientific quality.

Many other journals of various and varying standards have appeared, and to-day the list of monthly medical journals in India must run into some dozens.

### *The Indian Medical Gazette*

Since it was first published the *Gazette* has probably had its ups and downs, but these are scarcely reflected at all in its pages. It has shown a slow but steady expansion from the beginning; the first half dozen volumes had 20 to 24 pages in each number; in 1873 there were about 28 pages; in 1885 the number rose to 32; from 1895 onwards each number usually had 40 pages and occasionally the number rose to 48, but from the beginning of the century it appeared to fall back slightly to a steady 40, until 1922 when another advance was made to 48 and then to 52 pages; in 1928 the number rose to 60 and in 1936 to 64 pages in each issue. There has never been any suggestion that at any time contributions were difficult to obtain, nor is there any sign of 'padding'. The Indian medical periodicals of the early part of the last century, though scholarly, and often abounding in Latin quotations, usually made dull reading and consisted of little more than a series of case notes, but the *Gazette* introduced a more lively atmosphere. Admittedly case notes were numerous, but they did not predominate, and the *Gazette* was much more of a journal, on the lines of the *British Medical Journal*, its senior by just 25 years, or the

older *Lancet*, than its predecessors in India had been. Changes in character have been slight and have been the direct outcome of a change of scientific environment.

The format of the first number was almost the same as the current one, and the price was Re. 1-8 for a single copy as it is to-day, but the monthly subscription was a little higher. This is not surprising, for as late as 1885 the number of annual subscribers was only 141. The first page was not unnaturally devoted to an introduction stating the aims of the paper. 'Original communications' followed, and in this first number these consisted only of seven case notes on various subjects, e.g., syphilitic cirrhosis, atelectasis pulmonum, and a hermaphrodite, and a statistical statement on the treatment of tetanus in the Medical College, Calcutta. The next communication is headed 'Cases from Practice', in which four cases are reported by one writer; the distinction between this, the previous section, and a later one is not clear. The next page, 6, corresponds to our 'editorial' page and in later numbers comes about the middle of the number, as ours usually does now. The 'editorials' were on 'Professional Co-operation', which was really a request for contributions 'to satisfy the ever-craving appetite of the reading public' (the editor to-day is more troubled by the ever-increasing output of the writing public), on the cholera Congress at Constantinople, in which a demand was made that India should 'send her wise men also', on Indian medical warrants and civil pay, and on Indian ethnology, which included what we should call to-day an *open* letter from Joseph Fayrer to the Council of the Asiatic Society, suggesting an ethnological exhibition. The next section was 'Reports on Hospital Practice' (the word 'Mirror' was introduced in 1872), twelve more case reports and another statistical statement. Under the heading 'Reviews' is a long discussion, which is continued in the next two numbers, on a report on leprosy issued by the Government of India, by C. Macnamara, a frequent contributor and later editor. In this number there were no 'reviews' in the sense in which we use the word now (perhaps wrongly), but in later numbers there is a heading 'Short Notices of Recent Books' which corresponds to the present 'Reviews' section.

The next section is a very interesting one from a contemporary point of view. It is headed 'Pharmacopœia of India'. The opening paragraphs are quoted *in extenso*.

'The profession is doubtless aware that Dr. Waring, of the Madras Medical Service, so well known for the interest which he has always taken in the development of indigenous drugs, and for his invaluable "Manual of Therapeutics", is now in England, engaged on the part of Government, in the preparation of a Pharmacopœia for India. The following lists of Indian medicinal plants have lately been received in this country, and circulated amongst those from whom it is probable that information may be derived. With a view to give [sic] the subject still wider publicity, and

to invite general co-operation, they are now published in these columns. The subject is one, financially and commercially, of the utmost importance. £20,000 are annually expended in the importation of European drugs to India, whilst the country contains effective substitutes, valuable even as simple native preparations, but which, properly prepared, might be obtained at little more than half the cost of the European importation and yield a considerable profit to speculators. To take a single instance, one of many—Gallic acid costs the state 12s. 1½d. a pound. About £80 sterling are expended annually in the supply of 130 pounds weight of the drug, which, if manufactured from mango seed, would cost about eight annas a pound; being Rs. 65, instead of Rs. 800 for the year's requirements.

We venture to indulge the hope that another septennial period will not pass away without our seeing the establishment of large chemical laboratories in each presidency—not mere repositories for the reception and distribution of imported drugs, or for the manufacture of a few tinctures, but pharmaceutical workshops on an extended scale, with highly qualified practical English chemists attached to them—men who would analyse and test the products of the country; and make preparations, of what was valuable, in the most efficient way.

Government might well initiate such a system, leaving it for completion, as they have done tea cultivation, to the enterprise of companies or of individuals. Information is solicited, meanwhile, on the subject of each indigenous product referred to in the two following lists.

Delete the word 'English', change the figures, and this might have been written to-day. Not 7 but 70 years have passed, and we are little nearer this goal.

The first list is headed 'Principal Medicinal Plants, etc., of India', and the second, 'The Medicinal Plants, etc., of India. The Properties of which Appear Deserving of Further Investigation'. There is then a list of indigenous plants prepared by Baboo Kanny Loll Dey, this includes *Plantago ispaghula*, whose medicinal properties are described as 'demulcent and emollient. Employed with best advantage in chronic diarrhoea and dysentery, and in all inflammatory affections of the mucous membrane of the alimentary canal' (*vide* p. 733 of the present number).

The number ends with 'Extracts from European Journals' ('Current Topics' from 1880), and 'Correspondence'. In the second number the journal is obviously finding its feet for in the original communications section the case reports are replaced by original articles—on linear extraction (by C. Macnamara), the pathology and treatment of cholera, the physiological effects of quinine, etc.

Two other paragraphs from the first volume are interesting. C. Macnamara, again, in a paper in which he reports the remarkable efficacy of ipecacuanha in dysentery but complains of its 'nauseous' taste, makes the following suggestion.

'It occurred to me, therefore, that the active principle of ipecacuanha, called emetina, might perhaps be substituted for the powdered root of the plant, in the same way that quinine is given instead of bark. Since last December I have administered emetina in several cases of dysentery, and it appears to exert exactly the same effect as ipecacuanha in controlling the disease; one grain corresponds to about 20 of ipecacuanha, and it

may be administered in the form of pills, or mixed with a little acidulated water.'

In the same number an editorial on cinchona alkaloids contains the following:—

'But the inquiry into medicinal efficacy of Cinchonidine, Quinidine, and Cinchonine, apart from its professional importance, is one of wide and general interest; for it bears very materially upon the extent of the success of Cinchona cultivation in India. If these principles proved to be, as supposed, even *nearly* [original italics] as efficacious as Quinine, the value of the high percentage of alkaloids in the Neilgherry Cinchonas will be considerably enhanced. If, on the other hand, their medicinal action is found to be much inferior, the commercial importance of these cinchonas will necessarily diminish in proportion. The medical officers engaged in this inquiry need hardly therefore be reminded how great a trust is reposed in their hands: upon their verdict will depend the settlement of an important medical and commercial question.'

It has been repeatedly shown that the other cinchona alkaloids are *nearly* as efficacious as quinine, yet the Neilgherry plantations were allowed to fail and the monopoly to go to Java, though the same line of argument has been used again and again in these pages and as recently as June 1938. Medical science has made remarkable advances in the last 75 years, but it has also shown a remarkable tendency to go round in circles; this is particularly the case where its natural progress has been impeded by failure of outside agencies to render it the support which it might legitimately expect.

#### *The Editors and Publishers*

The editors of the *Indian Medical Gazette* from the beginning until a few years ago were all members of the Indian Medical Service, with one exception, W. J. Simpson, Health Officer of Calcutta, who edited the journal alone for 4 years, from 1894 to 1897, though his name appears as editor in association with members of the service from 1889. The last service editor was Robert Knowles, who resigned at the end of 1932, on account of ill health. D. Boyes Smith was the first editor; he was afterwards professor of medicine at the Medical College, Calcutta, and later principal, and when he retired he became professor of military medicine at the Army Medical School, Netley.

Kenneth McLeod became editor in 1871 in association with C. Macnamara; both were apparently dynamic personalities; the former continued to edit the journal for 20 years, and even after his retirement was a regular contributor. Under his editorship the journal flourished and took up an established position in world medical literature from which it has never receded. He was followed by W. J. Simpson, referred to above, and then by W. H. Buchanan (later Sir Walter Buchanan) who except for periods of leave held the editorship for 19 years. After an intermission of 2 years during which David McCay was editor, J. W. D. Megaw (later Sir John Megaw), the director of the School of Tropical Medicine, Calcutta, took over the editorship and the journal entered on another flourishing stage of its career. The



increased demand on its space was met by a change in type and the addition of a number of pages, which necessitated the appointment of an assistant editor, and R. Knowles was appointed in 1923; he succeeded Sir John Megaw in 1928 and was editor until the end of 1932 (v. s.). Since that date, L. Everard Napier, who became assistant editor in 1928, has edited the journal, and P. A. Maplestone has been assistant editor. A list of editors is appended.

At one period the names of associate editors, usually one in Bombay and one in Madras, appeared on the title page of the volume. The object was of course to give the journal a less local character; this manœuvre which was in our opinion not necessary and in practice was never a success, the associate editorship being of necessity purely nominal, was finally dropped in 1922.

The editors have always been men actively engaged in some branch of medical science, but their fields of activity have varied considerably; the first editor, D. Boyes Smith, was a Fellow of the Royal College of Physicians, as is the present one; three others C. R. Francis, D. McCay, and W. J. Simpson have been members. Boyes Smith was a professor of medicine at the Calcutta Medical College, as also was D. McCay; J. W. D. Megaw, who later became Director-General, Indian Medical Service, was professor of tropical medicine at the School of Tropical Medicine, as is the present editor; R. Knowles was the professor of protozoology at this School. Kenneth McLeod, a Fellow of the Royal College of Surgeons of Edinburgh (apparently at the age of 20) and later an Honorary Fellow of the Royal College of Surgeons of England, was professor of surgical anatomy and clinical surgery, and later of surgery at the Medical College; C. Macnamara was professor of ophthalmic surgery and L. A. Waddell, professor of chemistry at the same college. W. J. Buchanan did not hold any academic appointments; he was in the jail department and became Inspector-General of Prisons, Bengal, in 1913 and was later knighted. W. J. Simpson was, as we have said, health officer of Calcutta.

The first sixteen volumes were published by Wyman & Co., the next three by Newman & Co., and in 1835 the *Gazette* was taken over by Messrs. Thacker, Spink & Co., who have published it since. Mr. C. F. Hooper, who was first associated with the *Indian Medical Gazette* in 1891, took over the management early in this century, and did much to improve the journal and expand its subscription list. 7

#### Policy

The *Indian Medical Gazette* has no 'platform', and its only policy is the furtherance of medical science. It does not even claim any special mission in furthering the interests of the practitioners of scientific medicine, though it has these at heart, for we believe that they will further their material interests best by ever advancing their science and perfecting them-

selves in the application of it to the relief of human suffering. Moreover, the interests of different sections of the medical community often appear to be divergent, and it has never been the policy of this journal to further the interest of one particular section of this community, though, from time to time when special injustices appeared to exist or to be imminent, it has felt compelled to protest, but, we believe, never selfishly, for, though most of the editors have been members of the Indian Medical Service, editorial support has usually been given on behalf of the lower grades of the medical services, such as the sub-assistant surgeons. If in the past the rule of avoiding partisanship, or even discussing controversial subjects of a political nature, has occasionally been broken, this has not occurred for many years, and never, we claim, under the present régime.

We have emphasized above that the *Gazette* is an all-India journal and that its contributions come from, and its readers live in, all parts of India; similarly, in the selection and priority of contributions we show no bias in favour of any race or creed, of any service, or of the holders of any particular qualification, for the contributors are Indian, British, and foreign, members of the I.M.S., I.M.D. and provincial services, railway, tea-garden and other industrial medical officers, and private practitioners, and articles by L.M.F.s and F.R.C.P.s, by M.D.s of London, of New York, and of Patna, and, we will add, even to-day, of Hamburg, all appear side by side. If in the past the journal has enjoyed some measure of success, we feel that it is due very largely to this liberal policy.

#### The Future

The last twenty years have seen considerable expansion and all-round improvement in this journal, but we are not content to leave it at that. The success of a journal depends to a great extent on its editors, publishers and printers, but to a greater extent on its contributors and its readers. This journal has a wide circulation, but, with an even wider one, it could afford to add more pages and institute other improvements. This is a matter in which we ask the co-operation of our present subscribers, for their own benefit.

The *Indian Medical Gazette* can look back on 75 years of very useful life, and, if civilization survives the ordeal through which it is now passing, as every omen is favourable, we are confident that the *Gazette* can look forward to a particularly bright future.

#### List of Editors and Assistant Editors of the *Indian Medical Gazette*

- D. B. Smith, 1866.
- J. A. P. Colles, 1867.
- C. R. Francis, 1868.
- J. T. Carter Ross, 1869 to 1870.
- N. C. Macnamara, 1871 to 1873.
- K. McLeod, 1871 to 1892.
- J. G. French, 1876 to 1877.

L. A. Waddell, 1884 to 1885 and 1897 to 1899.  
 W. J. Simpson, 1889 to 1897.  
 A. Crombie, 1892 to 1893.  
 D. M. Moir, 1897 and 1903 to 1904.  
 C. H. Bedford, 1897.  
 F. P. Maynard, 1898.

W. J. Buchanan, 1899 to 1918.  
 D. McCay, 1909 to 1910 and 1919 to 1920.  
 J. W. D. Megaw, 1921 to 1928.  
 R. Knowles, 1923 to 1932.  
 L. E. Napier, 1928 to date.  
 P. A. Maplestone, 1933 to date.

## Special Articles

### HÆMATOLOGICAL TECHNIQUE

#### PART VI

By L. EVERARD NAPIER, F.R.C.P. (Lond.)

and

C. R. DAS GUPTA, M.B. (Cal.), D.T.M.

(From the Calcutta School of Tropical Medicine)

#### *The making and staining of blood films*

PROPERLY made and well-stained blood smears are essential for the white cell differential count, the enumeration of the nuclear lobes of neutrophil polymorphonuclears, as in the Arneth and Schilling counts, and also for the determination of the red-cell size by the Price-Jones' method.

For ordinary work blood films are made on 3-by-1-inch glass slides and for special studies on 2-cm.-square coverslip: only new slides and coverslips should be used if this is possible. The slide and the coverslip must be thin, completely transparent, scrupulously clean, and free from grease and dust.

#### *Cleaning glass slides and coverslips*

Place the slides and coverslips in sulphuric-acid-bichromate mixture\* and allow them to remain for twenty-four hours; this mixture should be kept in a large jar for the slides and in a small one for the coverslips. Decant off the cleaning mixture into another similar glass jar, which is then ready for use again. Transfer the slides or coverslips to a shallow enamelled tray or a big petri dish, and place this under a tap for 3 to 4 hours, stirring from time to time with a glass rod. Finally, wash with distilled water, dry with a piece of soft linen, and put them in a jar of absolute alcohol for twenty-four hours (methylated spirit may be used as a substitute). With a pair of forceps take out the slides or coverslips one by one, allow the excess of spirit to drain off, flame in a bunsen or spirit lamp, clean again with soft linen, and store in a dust-proof container—in a slide box for the slides and in a small petri dish for the coverslips. These are now ready for use for all ordinary work.

* Concentrated sulphuric acid	..	500 c.cm.
Potassium bichromate (powdered)	..	100 gm.
Water	..	.. to 1 litre

#### *Polishing the slides*

For special work, polish one side of a slide, cleaned as above, with jewellers' rouge for 2 to 3 minutes, clean with soft linen (selvyt cloth or silk is the best for this purpose), mark the polished side with a glass pencil, and store for future use in a dust-proof container.

#### *A. Spreading the film in the routine use of venous blood*

(i) *On slides.*—Put a few polished slides on a flat surface. With a syringe collect the blood from a vein (*vide* part I). Before putting the blood into the oxalated flask and while the needle is still attached to the syringe, put a small drop of blood on to the middle of the slide, a little away from the end. Apply the thin edge of another slide, with the corners cut off so that the spreading edge is narrower than the slide, or better still of a spreader (hæmocytometer coverslips make excellent spreaders on account of their smooth narrow edge), to the middle of the glass slide, slide it along until it makes contact with the drop of blood which will now spread along the edge of the spreader (slight lateral movement will accelerate this), then with the spreader at an angle of about 30° to 40° to the slide, push the spreader with the blood following it along the slide and raise the spreader abruptly just before the whole drop of blood has been used up. The film should be dried quickly by waving it in the air, or under an electric fan. An ideal film should occupy the middle third of the slide, should be of uniform thickness, should not have any tails, and when viewed under the microscope the red cells should just touch one another and there should not be any rouleau formation anywhere on the slide.

Fig. 1a shows a satisfactory film but with 'tails', and figure 1b a good film with a straight 'leucocytic edge'. They were drawn from above downwards. Figure 2 shows the low-power view of a satisfactory leucocytic edge; the leucocytes are actually discrete though the photograph scarcely gives that impression.

The important points are a perfectly clean slide, a good spreader, and a drop of blood of the right size; this last can only be gauged by trial and error, but, compared with the size of the drop required from a normal individual, a larger drop will be required from an anæmic patient

and a smaller drop from one with polycythemia or leukaemia.



a

Fig. 1.

b



Fig. 2.

(ii) *On coverslips.*—Place a few clean coverslips on a flat even surface. Proceeding as in (i) put a very small drop of blood on the centre of a coverslip; place another clean coverslip of the same size on the top of the drop of blood in such a way that the sides of the two coverslips are not opposed (see figure 3). If the two coverslips are clean, the blood will spread uniformly between them. Now draw apart the coverslips quickly but gently, and dry them quickly by waving them in the air or under an electric fan.

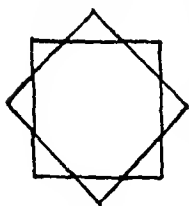


Fig. 3.

### B. From capillary blood from the finger or ear lobe

Prick the finger or ear lobe fairly deeply with a sharp surgical needle or with a blood gun, so that the blood flows freely from the wound. Apply the surface of a clean slide or coverslip to a small drop of blood and proceed as in A (i) or (ii).

#### Comparing the two methods

The method of choice is in our opinion the slide smear. The advocates of the coverslip method claim that it is the only way to obtain an even distribution of cells and that consequently reliable differential counts can only be made from coverslips. On the other hand, it is much easier to make a good film on a slide, and, if the whole drop of blood on the slide is utilized in making the smear and this drop is a small one, examination of such a smear will give as reliable information as examining a coverslip smear, the preparation of which demands considerable dexterity.

#### Staining blood films

All blood smears should be stained within twenty-four hours. If the smears cannot be stained immediately they must be fixed with methyl alcohol and stored in a dust-proof slide box for staining at a later date. The unstained slides must never be left uncovered on the working table as blood is readily eaten by the flies during the day and by cockroaches at night.

Romanowsky stains are used for all blood work. The most commonly used stains are those originated by Leishman, Wright, Jenner, and Giemsa. All these stains depend for their action on the compounds formed by the interaction of methylene blue and eosin, and the differences between the various stains are due to the proportion of the two stains. Excepting Giemsa's stain, the fluid stains are prepared by dissolving the dry powder in acetone-free pure methyl alcohol, so that a preliminary fixation with methyl alcohol is only required in the case of Giemsa's stain. Leishman's and Wright's stains are used in the strength of 0.15 per cent, and Jenner's stain in the strength of 0.5 per cent.

#### Preparing Leishman's, Wright's and Jenner's stains

Stains in powder or tablet forms and extra-pure acetone-free methyl alcohol for dissolving the stains should be obtained from some reliable firm. We have found the Gürr's\* stains to be very satisfactory.

All the glassware used in preparing the stains and in storing them should be scrupulously clean, and free from any trace of water; they should be rinsed first with absolute alcohol and finally with a little methyl alcohol.

Take the requisite amount of stain in powder or tablet form in a small glass mortar. Measure

\* George T. Gürr, 136, New Kings Road, London, S.W.6, England.

out the requisite amount of methyl alcohol in a graduated glass cylinder. Pour out about 2 c.cm. of methyl alcohol on the stain and grind well to make it into a thin paste. Add in small quantities at a time about half the total amount of methyl alcohol, grinding all the time. Carefully decant the supernatant dissolved stain into a clean glass stoppered bottle. Add more methyl alcohol to the undissolved stain, grinding as before. Again decant the supernatant stain into the bottle, continue the process until all the methyl alcohol is used up. If this is properly done all the stain will go into solution and no residue will be left at the end. Incubate the bottle with the stain at 37°C. for 24 hours when it will be ready for use.

#### A. Staining with Leishman's, Wright's or Jenner's stain

##### Reagents and apparatus required

1. Prepared stain, preferably in a drop bottle.
2. Distilled water (pH 7.0), or buffer solution with pH of 6.4 and made with acid monopotassium phosphate and disodium phosphate\*.
3. Fresh distilled water which is slightly acid in reaction.

4. Staining rack. This can be made with plasticine and a pair of glass rods of equal size and thickness, and may be placed at one end of a sink away from the water tap, or on a rectangular enamelled tray placed near a tap.

Glass beakers, cylinders, a pair of forceps, capillary pipettes, teats, etc.

**Technique.**—Put the slides on the staining rack taking care that the side with the blood film is upwards; also see that the two ends of the slides are in the same plane.

From a drop bottle, or with a pipette, pour on sufficient stain to cover the whole of the film; wait for one minute to allow for proper fixing; with a capillary pipette now add distilled water (pH 6.8 to 7.0) or the buffer solution—the same volume in the case of Leishman's and Wright's stains but double the volume in the case of Jenner's stains. With a capillary pipette or glass rod thoroughly mix the stain with the diluent to ensure a uniform mixture over the film.

When the mixture is allowed to settle, a scum will form on the top, if the proportion of the stain and diluent has been correct. According to the depth of staining required, allow the diluted stain to act for 5 to 10 minutes, in the case of Leishman's and Wright's stains, and 3 to 5 minutes, in the case of Jenner's stain.

The diluted or undiluted stains on the slides must not be allowed to dry up at any stage of the staining. Drying is prevented by covering the staining rack with a wide bell-jar, or other improvised device†.

* Monopotassium phosphate	.. 6.63 gm.
Anhydrous disodium phosphate	.. 2.56 gm.
Distilled water	.. up to 1 litre
Add 1 c.cm. of chloroform as preservative.	

† The precaution will seldom be necessary in humid climates, e.g., of Bengal and Assam, except in the hottest months, but will be imperative in drier provinces in India, and in other dry countries such as Iraq, Egypt, etc.

When the staining is complete, hold one end of the slide firmly with a pair of forceps, and place the stain-flooded slide under a running tap. This will wash off all the stain from the upper surface, while the bottom is cleaned by rubbing it well with the fingers of the left hand. The slide is now transferred to the beaker containing fresh distilled water and gently shaken to and fro till the colour of the smear becomes faintly pink. Now take it out of the beaker, wash again under the tap and allow it to dry. In order to dry it without allowing dust to adhere to the stained surface, the slide should be sloped against a vertical surface, e.g., a wall or the side of a box, with the film side inwards. (It is scarcely necessary to point out that heat should not be applied to a blood film at any stage in its preparation.)

When it is dry the slide is ready to be examined.

#### B. Staining with Giemsa's stain

It is more difficult to prepare this stain and it is better to purchase it in solution. Giemsa's stain as prepared by Gürr is quite satisfactory.

In staining with Giemsa's stain, preliminary fixing with methyl alcohol or some other fixing stain is absolutely necessary.

##### Preparing dilute solution

Take about 20 c.cm. of prepared distilled water (pH 7.0) or buffer solution in a clean transparent glass cylinder, add 20 drops of undiluted stain, or in other words as many drops of stain as there are cubic centimetres of water. Mix well by inverting the cylinder and see that the depth of colour of the mixture is such that, when held in front of the eyes, it allows a distant object to be seen through it.

(i) Place the slides to be stained on a staining rack, flood the slide with methyl alcohol and cover with a bell-jar, so that the methyl alcohol does not dry up on the slide. Allow the methyl alcohol to act for about two minutes, remove the jar and thoroughly wash with distilled water.

Now flood the slide with the diluted stain, cover with a bell-jar, and allow the stain to act overnight. Next morning wash and dry the slide as in A.

#### (ii) Combined staining with Leishman's, Wright's or Jenner's and Giemsa's

This is done exactly in the same way as in A but substituting the dilute Giemsa's stain as the diluent in place of distilled water or buffer solution.

#### (iii) Combined staining with May-Grünwald\* and Giemsa

Pour on undiluted May-Grünwald's stain just sufficient to cover the slide, place a bell-jar over the staining rack, allow the stain to act for 2 to 3 minutes, remove the bell-jar, and add an equal amount of neutral distilled water (pH 7). Allow

\* This can be purchased in solution and is available from G. T. Gürr (v.s.).

## MAKING PLASMA SAFE FOR TRANSFUSION

By S. D. S. GREVAL

LIEUTENANT-COLONEL, I.M.S.

Imperial Serologist, School of Tropical Medicine,  
Calcutta

THE intention is, (i) to state that it is not safe to give a transfusion of incompatible plasma, (ii) to suggest means of making the plasma safe, (iii) to indicate how stored plasma helps in transfusions, and (iv) to indulge in two speculations regarding the use of plasma in malignant growths.

### I. Incompatible plasma

A disaster in blood transfusion, occurring with dramatic suddenness, when an error in grouping blood has been made, is due to lysis and/or agglutination of the donor's corpuscles in the recipient's body. The donor's plasma, however, is not without effect. If it has not been made ineffective by dilution with the recipient's plasma it will lyse and/or agglutinate the recipient's corpuscles. This is known to occur when a dangerous 'universal donor' has served a recipient of a group other than O. His own corpuscles are inagglutinable; the effect produced is entirely due to the action on the recipient's corpuscles of the isohæmagglutinins in the donor's plasma.

If the danger from the plasma of a subject of group O is real then the danger from the plasma of subject A for subject B, from the plasma of subject B for subject A, and from the plasma of both subjects A and B for subject AB is also real. The writer holds that the danger from a dangerous 'universal donor' is real (Grevall and Chandra, 1939).

The risk from incompatible plasma would in fact be increased if the titre of sera a (from subjects B; III Jansky and Moss) and sera b (from subjects A; II Jansky and Moss) were of the same high order as that of sera ab (from subjects O; I Jansky and IV Moss). Such is

(Continued from previous page)

the diluted stain to act for 5 to 10 minutes according to the depth of staining desired, wash thoroughly with neutral distilled water and then flood the slide with dilute Giemsa's stain to act for 15 to 30 minutes according to the depth of the staining desired, and wash and dry as in A.

### Methods used in our laboratory

For all ordinary work Wright's staining method is used, and for special work, e.g., examining smears from the marrow, counting the nuclear lobes in Arnetz and Schilling counts, combined May-Grünwald and Giemsa's staining are preferred. For, with the combined May-Grünwald and Giemsa's staining, all the component parts of both mature and immature red and white cells are very well shown.

not the case. On the whole the isohæmagglutinins a and b in sera a and b are weaker than in sera ab. But sera a and b of high titre are found. The writer uses only these sera in grouping tests. A simple scheme for titrating the sera and excluding the risk has been given in the communication quoted in the last paragraph.

### II. Making plasma safe

Although the danger of injecting ungrouped plasma intravenously has not been plainly admitted, ideal plasma has been described and methods of making plasma (other than ideal) safe have been recommended and adopted. Plasma from subjects AB (Jansky IV and Moss I) having no isohæmagglutinins has been considered ideal (Editorial, *B. M. J.*, 1940). Bloods A and B have been taken in the same bottle to remove the isohæmagglutinins by absorption (Edwards, Kay and Davie, 1940). Plasma has been diluted with an equal volume of normal saline (Goldman, 1940; Smith, 1940). There are difficulties in obtaining the ideal plasma and in making the one other than ideal safe according to the devices mentioned. Subjects AB are scarce, absolutely, all over the world. Subjects B are scarce, relatively, in Europe and America; for every A a partner B cannot be found to fill the same bottle. Citrated plasma is likely to coagulate at times when diluted with an equal volume of normal saline and loses half its value always.

Davie (1940) who started by taking for storage, plasma from the blood of subjects of group 1 (Moss 1 or I, International AB) only now also takes it from the blood of subjects of group 2 (Moss 2 or II, International A). The latter plasma given after dilution with an equal volume of saline, without regard for the group of the recipient, is not likely to do much damage in England where the predominating groups are O and A. Besides, the isohæmagglutinin b it contains is likely to be, on an average, of a lower titre than the isohæmagglutinin a (from plasma of subjects B, Moss 3 or III) would be and may not affect an odd recipient of group B (Moss III) or AB (Moss I). Plasma from subjects of group 3 (Moss III, B) will not be so safe. In India, where O, A, and B are more evenly distributed, risk would be real. The nomenclature, outside the brackets, in this paragraph is of the original communication. The brackets give the writer's explanation and international nomenclature.

Incidentally, the risk will persist even when the plasma is given intraperitoneally or intramuscularly to an infant with a view to increasing the volume of blood in the circulatory system rapidly.

The writer recommends the following plan for selecting plasma which is safe, with respect to its isohæmagglutinin content, or making dangerous plasma safe:—

1. *Selection of safe plasmas.*—Plasma conforming to the standard of the safe universal



donor (Greval and Chandra, *loc. cit.*) with respect to the titre of isohæmagglutinin a and b is safe. Plasma ab (from subjects O) is thus selected. Plasma a (from subjects B) and plasma b (from subjects A) are selected similarly. Plasma o from subjects AB is of course ideal.

2. *Mixing of plasmas.*—Plasma a and plasma b may be a trifle over double the safe strength if they can be mixed in equal volumes. After mixing and keeping a day in the cold the titre will be found to be below the arithmetically calculated titre and safe. The arithmetically calculated titre of course will be half the previous titre of each isohæmagglutinin.

In India the discrepancy between groups A and B is not so marked as in England although group B predominates slightly. In a blood transfusion centre in a big town it is possible to get both the groups in about the same number. There will be as many bottles of stored A blood as of B blood. So far as the writer's experience of the titre of the sera goes, a great majority of the plasmas a and b can be made safe by mixing.

3. *Removal of isohæmagglutinin by absorption.*—Two time-expired (over 10 days old) bottles of bloods A and B, plasma from which is not safe to begin with and cannot be made so by mixing, are taken and termed first and second bottle. A third empty bottle is added. The supernat from the first bottle is transferred to the third bottle by a sterile system of two rubber tubes, a two-way adapter and a syringe. The supernat from the second bottle is then transferred to the first bottle by the same system and mixed gently with the deposit of red blood corpuscles. The supernat removed to the empty bottle is finally transferred to the second bottle and mixed with the deposit of corpuscles. Plasmas a and b are now in contact with the corpuscles A and B which will remove their isohæmagglutinins if kept at room temperature for 15 minutes and in the cold for half an hour. The agglutinated corpuscles fall to the bottom rapidly leaving a clear supernat which can be removed and bottled. A trace of colour can be disregarded.

For complete absorption of the isoagglutinins from a volume of plasma half a volume of corpuscles suffices unless the latter are A<sub>2</sub> or A<sub>3</sub> (slow A's). For a partial removal of the isoagglutinins even a smaller quantity will do.

The operation of removals and transfers must be performed with sterile precautions; or else the absorbed plasma will have to be filtered through a Seitz filter.

The agglutinated corpuscles are still either A or B although sensitized and available for making other preparations.

Dangerous excess of a or b from a serum ab can also be eliminated by suitable absorption. The entire contents can be removed by absorption with corpuscles AB from a subject AB.

4. *Dilution of plasma.*—If the devices described under 2 and 3 cannot be used the plasma

must be diluted to a safe strength *after its titre has been determined*. The diluting fluid should be 0.25 per cent sod. citrate in normal saline. The limit of safety of sod. citrate for an adult is 5 grammes.

Other dangers in plasma are those that also exist in stored whole blood. It might be thought that the danger from syphilis might be eliminated without the aid of a Wassermann test by filtering or drying plasma and thus removing or killing the spirochætes which may be present. The danger of a passive sensitization, however, brought about in a recipient by a syphilitic's blood remains: and sensitization accompanied by a subsequent assault is probably more important in the long story of syphilis than any immediate damage done by the spirochætes. The writer, therefore, does not recommend that the Wassermann test should be omitted.

Potassium ions are reported to increase in plasma when the whole blood is stored (Editorial, *J. A. M. A.*, 1939). Danger from them would be the same as the one arising from the use of the stored whole blood from which the plasma has been taken. This danger does not appear to exist. 'Data have been presented on the incidence and type of reaction occurring in a series of 1,458 transfusions of blood stored from one to thirty-eight days and 146 transfusions of fresh blood. No types of reactions were encountered that were distinctive of preserved blood' (DeGowin and Hardin, 1940). The blood had been taken in a sod. citrate solution for short storage and in a dextrose-citrate solution for long storage.

Incidentally, the plasma possesses all the advantages stored blood has over fresh blood. They are: (i) decrease in food and allergic reactions, (ii) extended observation on the state of health of the donor during an epidemic, and (iii) exclusion of blood of high coagulability in certain conditions (Greval, Chandra and Roy Chowdhury, 1940).

Plasma made safe by methods other than dilution can be dried for easy storage and transport. A method has been published (Davie, *loc. cit.*). On the whole, dried plasma has so far not been preferred to preserved liquid plasma. 'There was a place for dried plasma, but it could not replace plasma saline' (Davie, *loc. cit.*).

### III. Help given by stored plasma in transfusions

That stored plasma has a place in the treatment of sudden loss of blood has been discussed this year by different workers from different countries (Best and Solandt, 1940; Goldman, *loc. cit.*; Smith, *loc. cit.*; Davie, *loc. cit.*; Greval, Chandra and Roy Chowdhury, *loc. cit.*). That it prevents waste in a blood bank is also worthy of remark. One important consideration when blood is taken from voluntary, unpaid, public-spirited donors is that it should be made use of. Often, in a newly started blood bank,



blood taken for storage is limited to a bottle or two for each of groups O, A and B lest there should be no demand. Then the demand comes suddenly and there is no blood. All sudden demands can be satisfied wholly or partly by stored plasma for preparing which more bottles of blood can be taken for storage without fear of waste. Blood from group AB can also be taken, for the ideal plasma and for absorbing plasma of dangerous 'universal donors'. Ordinarily this blood is not taken.

#### IV. Two speculations regarding malignant growths

1. *Action of the isohæmagglutinins on malignant cells.*—An isohæmagglutinin is absorbed by all the cells of the body of a subject of the appropriate group. Will the rapidly-growing ill-formed malignant cells absorb it, become sensitized, and be adversely affected? Appropriate plasma or sera below a dangerous titre can be given intravenously. Even high-titre plasma or sera can be injected locally into the growth and applied as dressings.

2. *Possibility of replacing most of a patient's plasma.*—Normal humoral forces are probably capable of destroying malignant growths. Given a stock of compatible plasma, it should be possible to replace most of a patient's plasma in the course of a few days. The patient could be (i) transfused with compatible whole blood, (ii) bled and (iii) transfused with his own red blood cells and a healthy donor's compatible plasma. Steps (ii) and (iii) could be repeated. Will the replacement destroy the malignant growth?

#### Summary

1. Plasma may be incompatible like the plasma of a dangerous 'universal donor'.

2. Plasma stored for transfusion can be made safe by (i) selection, (ii) mixing, (iii) absorption and (iv) dilution. The Wassermann reaction should be done. Potassium ion concentration in the plasma is negligible if the red blood cells are removed in a few days. No distinctive reactions due to stored blood have

been recorded even after storage lasting 38 days.

3. The separation and storing of plasma will abolish waste in blood banks.

4. There are two speculations regarding the use of plasma in cases of malignant growths: (i) Will the appropriate isohæmagglutinin sensitize and destroy the malignant cells? (ii) Will the replacement of a patient's plasma by normal healthy plasma destroy the malignant cells?

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#### Addendum (dated 13th November)

Since this communication was sent, a report on the preparation of serum from plasma of stored blood has become available (Clegg and Dible, 1940). The serum is preferred to the plasma because of the formation of particulate matter in the latter on standing. It has a high calcium content (six to eight times normal) and is recommended for use regardless of the group of the recipient.

The present writer makes three observations: (1) His opinion on the danger of incompatibility of groups remains unchanged. (2) The risk of producing favourable conditions for the anaerobic flora, responsible for tetanus and gas gangrene, by increasing appreciably the calcium content of the tissues (Topley, 1933), needs consideration, particularly in connection with street accidents and war wounds. (3) Removal of the particulate matter from the plasma by filtering should not be difficult.

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## Medical News

### TUBERCULOSIS ASSOCIATION OF INDIA

#### TUBERCULOSIS NEWS

##### I. Tuberculosis Workers' Conference

THE second Tuberculosis Workers' Conference will be held in New Delhi from the 18th to 21st November, 1940. [The conference has now been successfully concluded.]

One whole day will be devoted to the discussion of the influence on the spread and development of tuberculosis of such environmental factors as poverty, over-crowding, under-nourishment and occupation of insanitary dwellings, and of the effects on the spread of tuberculosis of legislation including by-laws dealing with notification, erection of buildings, slum clearance, town planning and the regulation of lodging houses.

Other important subjects, such as tuberculosis surveys, uniformity of records of classification of patients and the results of treatment, will be discussed, as well as the interpretation of x-ray films and their recording. Further, a few clinical subjects dealing with the treatment of certain complications will also come up for debate.

The Conference will be opened and closed by Her Excellency the Marchioness of Linlithgow, President of the Tuberculosis Association of India.

##### II. Training Courses

The Tuberculosis Association of India, with the co-operation of the Bengal Tuberculosis Association, will organize a medical post-graduate course for training in

tuberculosis at the All-India Institute of Hygiene and Public Health, Calcutta, from the 15th January to 14th February, 1941.

2. The class will be limited to 30 registered medical practitioners—male or female—whether in Government service or otherwise. Ten seats will be reserved for practitioners in Bengal Province and 20 for candidates from other parts of India.

### III. Meetings

A central committee meeting of the Tuberculosis Association of India was held at the Viceroy's House, New Delhi, on the 28th October, under the presidency of H. E. the Marchioness of Linlithgow. Besides some routine matters, the following business was transacted. The committee approved the award of the Hassan Masud Suhrawardy Memorial Anti-Tuberculosis Challenge Shield for the all round good work on tuberculosis done during 1939 to the Madura Municipality which competed among 12 others. It was decided to request affiliated tuberculosis associations to send half-yearly (quarterly if possible) reports of their activities for incorporation in the tuberculosis news service of the central association. The committee also decided to proceed with the election of five members to the central committee from the affiliated associations. Finally, the committee resolved to offer to Dr. C. Frimodt-Møller, C.M.E. (Hon.), the present medical commissioner of the association, an extension of appointment by two years on the expiry of his present contract on the 30th April, 1941.

### IV. Tours

Lieutenant-General G. G. Jolly, chairman of the association, went on a tour of inspection to Bombay and Karachi during the second week of October and discussed with officers of the provincial tuberculosis associations the progress of anti-tuberculosis measures.

Dr. Frimodt-Møller, the medical commissioner of the association, paid a visit to Shillong on the 8th, 9th and 10th October to advise on the best tuberculosis scheme for Shillong and the province. He visited various proposed sites for a tuberculosis clinic and hospital at Shillong, and addressed a meeting of administrators and doctors held at Government House. While passing through Calcutta the medical commissioner discussed with the medical authorities of the B. N. and E. B. Railways how best they could co-operate in the anti-tuberculosis campaign.

### THE XVII ALL-INDIA MEDICAL CONFERENCE, VIZAGAPATAM, 1940

In connection with the scientific section of the forthcoming XVII All-India Medical Conference at Vizagapatam during the last week of December 1940, it is proposed to have symposiums in the following subjects in addition to the reading of papers:—

1. Surgery:—Surgical complications of filariasis.
2. Medicine:—High blood pressure, its ætiology, pathogenesis and treatment.
3. Obstetrics:—Maternal injuries of child birth.
4. Venereal Diseases:—Modern treatment of gonorrhoea.

The names of the openers of discussion on the above subjects will be announced in due course.

### LOCATION OF TUBERCULOSIS CLINICS

THAT if a tuberculosis clinic is to be of maximum benefit, it should be situated in, or as close as possible to, a thickly populated area, is the unanimous opinion of the committee of experts recently appointed by the Tuberculosis Association of India at the instance of the Government of India to consider what condition should govern the selection of sites for such clinics and whether any particular precautions were necessary in the case of clinics situated in populated areas.

The committee were also of the view that no particular conditions are necessary regarding the distance of a well-conducted clinic from the nearest house. They

recommended, however, that if a clinic is located in a part of a building used for other purposes, the clinic should have a separate entrance.

### FOR DISTINGUISHED SERVICE IN WAZIRISTAN

HIS IMPERIAL MAJESTY THE KING, EMPEROR OF INDIA, has been graciously pleased to give orders for the following appointment to the Most Excellent Order of the British Empire, for services rendered during the Operations in Waziristan, North-West Frontier Province:—

*To be an Officer of the Military Division of the said Most Excellent Order*

Lieut.-Colonel Robert Anceel Logan, I.M.S., Officer Commanding, No. 11 Field Ambulance, Waziristan.

### THE SULPHONAMIDE GROUP OF DRUGS IN THE TREATMENT OF PLAGUE

WE have received too late for publication in this issue, a paper from Lieut.-Colonel S. S. Sokhey, I.M.S., Director of the Haffkine Institute, Parel, Bombay, by himself, Dr. Wagle, and other members of the staff of this institution, on their results in the treatment of plague with anti-plague serum, sulphapyridine and sulphathiazole. The death rates in their three series were 28 per cent, 24 per cent, and 15 per cent, against 52 per cent, in the control series. The difference between any of the treated series and the control series is significant statistically.

The paper will appear in our next number.

### A SIMPLE METHOD OF OBTAINING ANÆROBIOSIS

WE have received an article by Major C. L. Pasricha, I.M.S., and Mr. S. K. Ghosh, of the School of Tropical Medicine, Calcutta, on this subject, for publication; it will appear in a later number. The main points are:—

A desiccator, or other suitable container which can be rendered air tight, is used; an ordinary tall glass tumbler covered with a petri-dish and made air tight with plasticine gives entirely satisfactory results, when only a small number of tubed cultures is to be incubated. Into the bottom of the desiccator are placed some moistened iron filings. There is a complete anærobiosis in about six hours. It is an advantage to evacuate the jar and then to admit hydrogen, but this is not absolutely necessary.

## Current Topics

### Hæmaturia from Sulphathiazole Therapy in Pneumonia

By JOHN H. ARNETT

(Abstracted from the *Journal of the American Medical Association*, Vol. CXV, 3rd August, 1940, p. 362)

THE tendency of sulphapyridine to form urinary crystals resulting in hæmaturia and even obstruction is by this time well known. Gross, Cooper and Scott have collected from the literature 36 cases of gross hæmaturia, with seven in which uroliths were specifically mentioned, complete bilateral ureteral block being disclosed at autopsy in one instance. Plummer and McLellan have reported two cases of unilateral calculus formation, one of which was fatal. Arnett, Shoup and Henry have reported a case of bilateral ureteral obstruction with recovery. The fact that similar complications can arise in the course of sulphathiazole therapy is now beginning to be recognized. Gross, Cooper and Scott have demonstrated concretions in the kidneys of rats receiving sulphathiazole,

# Prescribing a Laxative



WHEN, as frequently happens, the Physician is called upon to prescribe a laxative for prolonged personal use by the patient, Andrews Liver Salt merits special consideration. The main characteristics of this tonic laxative, listed below, suggest its wide range of suitability.

1. Andrews is pleasant tasting. All ages take it readily.
2. Andrews causes none of the griping or other discomforts which often create reluctance to continue the use of the more drastic purgatives. Its laxative action is due to the presence of magnesium sulphate and other salts, which increase the fluid content of the bowel by Osmotic action, and so lead to painless, easy evacuation.
3. Because of its natural and non-habit-forming action, Andrews—in suitable doses—may be taken with
4. every confidence by the physically weak and during pregnancy. This tonic laxative does not affect adversely the secretion of milk in nursing mothers. Indeed, the quantity of water taken with Andrews Liver Salt contributes to the extra liquids a nursing mother should take.
5. Andrews is particularly valuable in the case of patients liable to digestive trouble. The carbon dioxide which is liberated when Andrews is dissolved in water has a soothing effect on the stomach and a physical cleansing action on the stomach walls. Additionally, Andrews corrects excess acidity, stimulates the liver and promotes the flow of bile.
5. Andrews creates no dependence on artificial aid, but can be discontinued when the need for it ceases.

*Andrews Liver Salt increases the alkalinity of the body fluids and is, therefore, of great value in malaria and other feverish conditions for counteracting the excessive production of acid which takes place in such cases.*

## ANDREWS LIVER SALT

*A large size tin will be sent free on request, to any member of the Medical Profession.*

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# THE CALL OF PAIN

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and Pepper and Horack reported the death of a 77-year-old pneumonia patient who developed hematuria and oliguria while on sulphathiazole therapy. At autopsy the kidneys were found to be large and soft and their collecting tubules were dilated and contained crystalline material. In the case here reported severe hematuria and lumbar pain were present but the patient recovered.

It is the currently accepted belief that sulphathiazole, like sulphapyridine, may produce hematuria mechanically through the irritation caused by the crystals precipitated in the renal tubules and pelvis. No doubt the fact that in one present case, because of vomiting, it was impossible to maintain a sufficiently high fluid intake to prevent such precipitation was an important factor in causing the hematuria. The fact that such a complication may arise should not discourage the medical profession from using sulphathiazole, which is probably less toxic and more efficacious in cases of pneumonia than sulphapyridine. In 200 cases of pneumonia, half of which were treated by the former and half by the latter drug, Flippin, Schwartz and Rose report only one case of gross hematuria, and this occurred in the sulphapyridine group, while the mortality in the sulphathiazole group was lower by 3 per cent and vomiting was much less frequent. The point that should be emphasized is the importance of maintaining a sufficiently high fluid intake to prevent massive crystal formation. The fluid intake and urinary output should receive the watchful attention of the physician, and the urine should be examined at least daily for crystals and blood. If the intake can be kept in excess of 3,000 c.c. and the output at 1,500 c.c. or more a day, and if the drug is immediately discontinued and intravenous fluids are administered with the first appearance of lumbar pain or bloody urine, the dangers from renal complications will be reduced to a minimum.

### The Toxic Manifestations of Sulphanilamide and its Derivatives

By P. H. LONG,  
J. W. HAVILAND,  
L. B. EDWARDS,

and

E. A. BLISS

(From the *Journal of the American Medical Association*, Vol. CXV, 3rd August, 1940, p. 364)

It has become increasingly evident as time goes on that physicians often hesitate to use sulphanilamide or its derivatives because of a fear of the toxic manifestations of these drugs, while patients, because of their lack of appreciation of the possible toxic manifestations of this group of drugs, demand that the drugs be administered to them. These attitudes have at times brought about a somewhat peculiar situation.

It has seemed to us that physicians have been 'oversold' on the dangers connected with the use of sulphanilamide and its derivatives and that these drugs can be used with greater impunity than has hitherto been considered possible. It is for this reason that we have carefully analysed the incidence and types of toxic reactions occurring in hospitalized adults, 1,000 of whom were treated with sulphanilamide, 297 with sulphapyridine and 291 with sulphathiazole in the Johns Hopkins Hospital during the past few years. The results of this analysis are shown in the accompanying table.

It is obvious that certain deductions can be made from this group of patients in respect to the frequency and severity of the toxic manifestations of sulphanilamide or its derivatives, and we think that by a careful study of the clinical histories of these patients certain general conclusions can be drawn regarding the care of patients who are receiving these drugs.

In the first place it is to be noted that nausea and vomiting constitute a problem only as far as sulphapyridine therapy is concerned. We have noted that the more highly integrated the patient is, the greater the

chance that nausea and vomiting will occur in the course of therapy with sulphapyridine. In our Negro patients and in children, nausea and vomiting have caused little if any difficulty in the maintenance of therapy, but in the private wards this toxic manifestation has occasionally been a problem of grave importance. When severe nausea and vomiting occur, the fluid intake should be kept at a high level and sodium chloride administered either by mouth or parenterally in order to prevent dehydration and hypochloremia from developing.

Although adequate statistics are not available, it has seemed to us that dizziness is more common in the course of sulphanilamide therapy than when sulphapyridine or sulphathiazole is being used. The recognition that dizziness may occur is of great importance, especially with respect to patients who drive automobiles, perform heavy or light mechanical work, pilot airplanes or conduct other types of vehicles. All ambulatory patients who are receiving these drugs should be warned of the consequences that may arise from attacks of dizziness.

True toxic psychoses due to the drug are fortunately rare, but they may take almost any form; if a maniacal type of psychosis is present the patient should be carefully watched lest harm come to him. In general it is always best to stop the drug when such toxic manifestations arise. Neuritis, either peripheral or central, is fortunately very rare in the course of therapy with sulphanilamide, sulphapyridine or sulphathiazole, but if evidence of this toxic manifestation is noted the drug should be immediately stopped.

Cyanosis, either mild or severe, is very common in the course of treatment with sulphanilamide but is of little importance except possibly in older persons suffering from emphysema or any type of cardiac disease. In the course of treating lobar pneumonia with sulphapyridine we have never noticed that this drug contributed significantly to the cyanosis already present, and indeed we have repeatedly observed that successful chemotherapy was attended by a marked decrease in the degree of cyanosis present. Our experience with sulphathiazole leads us to believe that this drug produces minimal degrees of cyanosis.

Acidosis has not been reported in the course of sulphapyridine or sulphathiazole therapy, and in our experience it has practically been eliminated as a toxic reaction of sulphanilamide therapy by the concurrent use of sodium bicarbonate with each administration of sulphanilamide. We have never seen a clinical example of alkalosis produced by the administration of sodium bicarbonate in the course of sulphanilamide therapy.

Drug fever is an extremely common toxic manifestation in the course of sulphanilamide or sulphathiazole therapy. It may occur at any time from the first to the thirtieth day of treatment, but it is most commonly seen between the fifth and ninth day of treatment. Drug fever may be of three clinical types: a hectic remitting fever accompanied by chills of great severity, a steadily mounting fever and a low continuous fever. We are frequently asked to distinguish between the fever produced by the drug and the fever produced by infection. Since drug fever occurs most commonly from the fifth to the ninth day and since one expects the temperature of adequately treated patients to be normal by the third day, the appearance of fever, when all clinical signs are pointing toward a favourable termination of the disease, should immediately lead one to suspect that the rise in temperature is due to the drug and not to a recrudescence of the infection. Another factor of considerable importance is that when drug fever appears the patient begins to feel bad and almost always complains of headache and generalized malaise.

Simple drug fever in itself is probably not a dangerous toxic manifestation, but it has always seemed best to us to discontinue the drug if it makes its appearance. When the drug is stopped and fluids are vigorously forced, the temperature should return to normal within twelve to seventy-two hours, depending on the rapidity with which the drug is eliminated from the body. The slower the elimination of the drug, the more prolonged will be the fever.

Drug rashes are common in the course of sulphanilamide and sulphathiazole therapy but do not occur very often when sulphapyridine is being used. They may take any form, and we have seen crissipeloid, scarlatini-form, morbilliform, purpuric, erythema multiforme, papular, vesicular, pustular and nodular eruptions. In severe instances (especially if the drug is continued) the rash may progress to an exfoliating dermatitis. Rashes may occur at any time from the first to the thirtieth day of therapy. In a certain number of instances photo-sensitization of the skin seems to play a rôle in the production of the rash. For this reason patients who are receiving treatment with sulphanilamide or one of its derivatives should stay out of the sun until at least three days after cessation of therapy. A curious idea has recently become prevalent in this country, namely, that patients who have received sulphanilamide or one of its derivatives during the winter should keep out of the sun during the summer. There is absolutely no foundation in fact for this rumour.

Hepatitis characterized by jaundice without anaemia and a definite impairment of liver function has occurred in 0.6 per cent of patients who have been treated with sulphanilamide. This toxic reaction may occur early or late in the course of therapy. It has been noted that occasionally it accompanies dermatitis exfoliativa. In our experience the prognosis has been excellent if the drug is stopped immediately and fluids are forced, and as far as we know there has been no permanent impairment of liver function following recovery from this toxic reaction of sulphanilamide therapy. The

occurrence of hepatitis in the course of sulphapyridine therapy has been reported, but we have not seen it in our series of patients treated with this drug. As far as we know, hepatitis has not occurred in the course of sulphathiazole therapy, although it is to be expected.

Leukopænia with granulocytopenia may occur early or late in the course of therapy with sulphanilamide or its derivatives. In adults this toxic manifestation is relatively uncommon. We have noted a sharp drop in the leukocytes following a single dose of sulphanilamide in certain cases, and we have also noted that granulocytopenia may not occur until the sixtieth or seventieth day of treatment. Hence one must always be on the lookout for this type of toxic manifestation. It has been considered best to stop therapy with the drug if this toxic manifestation makes its appearance, but it must also be remembered that as far as we know there have not been any deaths reported from disturbances of the white cells during the first twelve days of therapy with any of these drugs.

Acute agranulocytosis is a rare complication of therapy with sulphanilamide and sulphapyridine and has not yet been reported in the course of therapy with sulphathiazole. This complication has in our experience occurred on the fourteenth or on a subsequent day of treatment with these drugs. The most common time for its appearance is between the seventeenth and the twenty-fifth day, although it may appear as late as the fortieth day of treatment. For this reason it is very important to check the white blood cell count at daily intervals on and after the

TABLE

*Manifestations of drug toxicity noted in hospitalized adults; 1,000 treated with sulphanilamide, 297 treated with sulphapyridine and 271 treated with sulphathiazole*

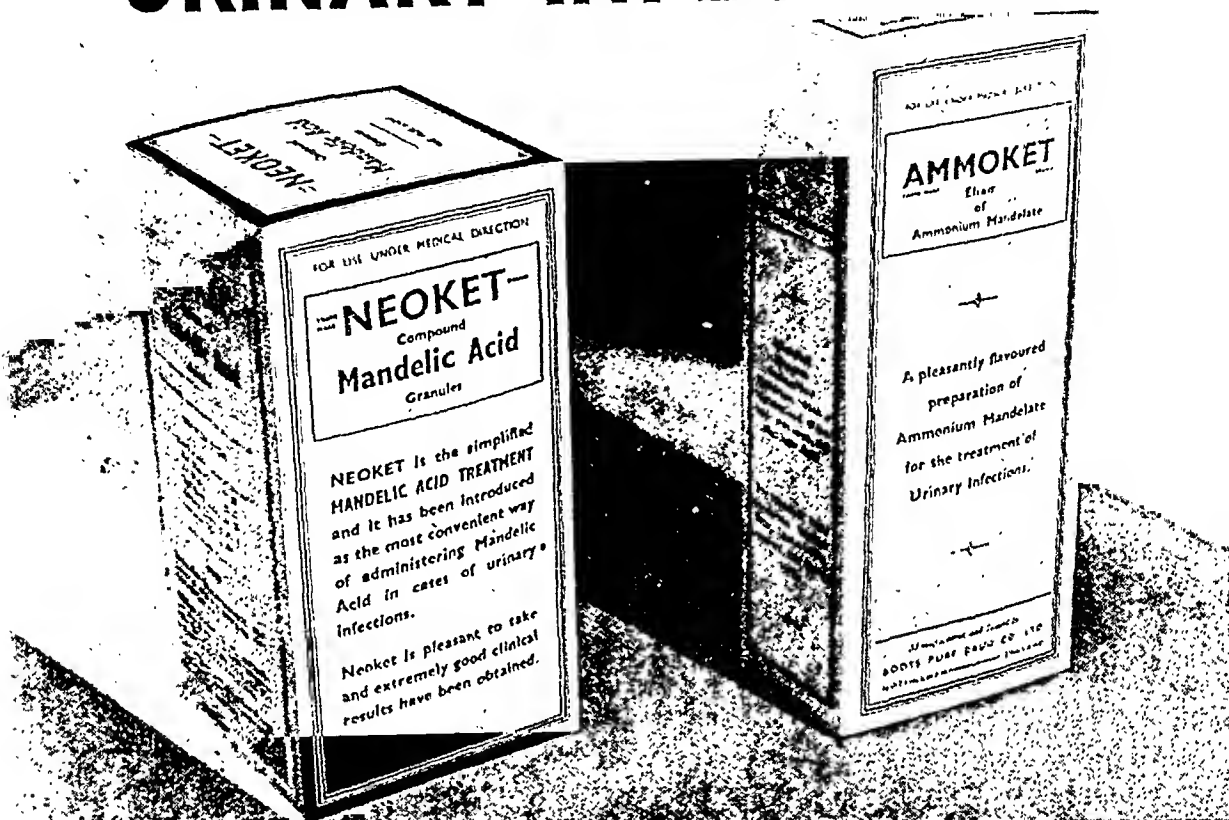
Reaction	Sulphanilamide	Sulphapyridine	Sulphathiazole
Nausea, vomiting ..	Fairly common	Frequent	Uncommon.
Dizziness ..	Common	Common	Uncommon.
Psychoses* ..	0.6%, occur early	0.3%, occur early	Not reported as yet.
Neuritis† ..	Very rare	Not reported	Not reported.
Cyanosis ..	Very common, early and late	Faint, common, early and late	Uncommon.
Acidosis* ..	1.9%, occurs at any time, rare if soda is used.	Not reported	Not reported.
Fever* ..	10%, generally 5th to 9th day, may occur 1st to 30th day.	4%, generally 5th to 9th day, may occur 1st to 30th day.	10%, generally 5th to 9th day.
Rash* ..	1.9%, may take any form, generally 5th to 9th day, may occur 1st to 30th day.	2%, may take any form, 5th to 9th day, may occur 1st to 30th day.	5%, nodular type common, may take any form, 5th to 9th day.
Hepatitis† ..	0.6%, early or late	Not seen, but reported	Not reported.
Leukopænia with granulocytopenia.† ..	0.3%, early or late	0.6%, early or late	1.6%, early or late.
Acute agranulocytosis† ..	0.1%, occurs 14th to 40th day, common 17th to 25th day.	0.3%, occurs 14th to 40th day, common 17th to 25th day.	Not reported.
Mild hæmolytic anaemia ..	3%, early and late	Rare	Not reported.
Acute hæmolytic anaemia† ..	1.8%, occurs 1st to 5th day	0.6%, occurs 1st to 5th day	Not reported.
Hæmaturia* ..	Not reported	8%, generally early	2.5%, generally early.
Anuria with azotæmia† ..	Not reported	0.3%, generally 1st 10 days	0.7%, generally 1st 10 days.
Hyperleukocytosis* ..	Generally in presence of acute hæmolytic anaemia.	Generally in presence of acute hæmolytic anaemia.	Not reported.
Injection of scleras and conjunctivas.*	Not reported	Not reported	4%, may occur with rash and fever, 5th to 9th day.
Purpura hæmorrhagica† ..	Not seen, but reported	Not seen, but reported	Not reported.
Ocular and auditory disturbances.*	Rare	Rare	Not reported.
Jaundice† ..	With acute hæmolytic anaemia or hepatitis.	With acute hæmolytic anaemia or hepatitis.	Not reported.
Painful joints* ..	Reported	Not reported	Reported with rash, etc.
Stomatitis* ..	Rare	Not reported	Not reported.
Gastro-intestinal tract disturbances.*	Bleeding rare, diarrhoea uncommon.	Rare	Not reported.

\* Best to stop drug and force fluids.

† Imperative to stop drug and force fluids.



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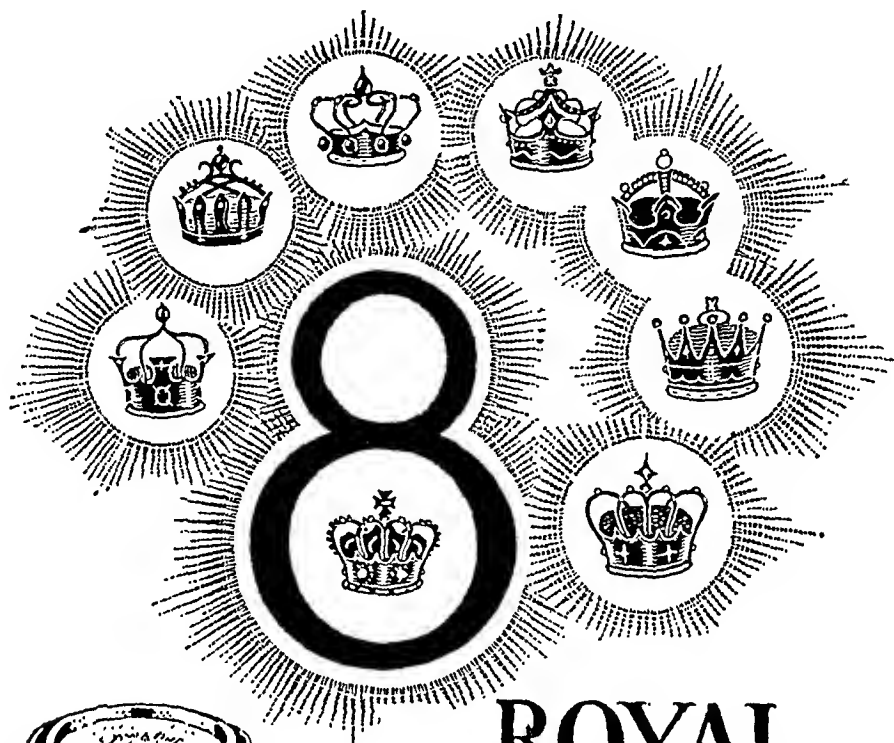
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twelfth day of treatment with sulphanilamide or its derivatives. If the white blood cell count drops and the polymorphonuclear leukocytes are decreased, it probably means the beginning of acute agranulocytosis. The drug should be stopped and fluids vigorously forced in order that the drug may be eliminated from the body as quickly as possible. Outside of this measure, it is probably unwise to attempt other therapeutic procedures designed to combat the agranulocytosis, except that we believe that it is a good plan to use transfusions when the haemoglobin content falls below 70 per cent. In our experience the prognosis of agranulocytosis occurring in the course of therapy with sulphanilamide and its derivatives is good if the toxic reaction is recognized in its inception.

Mild, slowly developing haemolytic anaemia, in which the haemoglobin content drops 20 per cent or more during the first ten days of treatment, has occurred in 3 per cent of the adult patients treated with sulphanilamide. This toxic manifestation is rare in the course of sulphapyridine treatment and has not been reported as yet in patients who are receiving sulphathiazole. In contradistinction to acute haemolytic anaemia, it seems to occur as frequently in white as it does in Negro patients. These mild anaemias should not be considered as alarming toxic manifestations, as they generally disappear when the drug is stopped and may be combated by the administration of 0.6 gm. of ferrous sulphate daily. In patients suffering from chronic osteomyelitis or other diseases in which it may be desirable to prescribe sulphanilamide over long periods of time, occasional transfusions will help to control these mild haemolytic anaemias.

Acute haemolytic anaemias occurred in 1.8 per cent of our adult patients who were treated with sulphanilamide and in 0.6 per cent of those who received sulphapyridine. It has not yet been reported in the course of sulphathiazole therapy. In practically all instances it makes its appearance in the first five days of treatment with these drugs and can almost always be recognized clinically by the sudden development of pallor of the mucous membranes of the mouth and conjunctivas. Mild jaundice almost invariably accompanies this toxic manifestation of drug therapy and is especially noticeable in the scleras. In very acute fulminating cases, haemoglobinemia and haemoglobinuria may be present. Urobilin is consistently found in the urine. We have seen patients whose haemoglobin content has dropped as much as 70 per cent within twenty-four hours when this toxic manifestation has made its appearance.

If possible, it is always best to stop the drug when an acute haemolytic anaemia is present. However, in certain cases of severe involvement in which the continuance of therapy has been a life-saving procedure, multiple transfusions have been used in order to maintain the red blood cell count until the critical period of the illness has passed and it is possible to stop the drug. In most instances it has been necessary to administer one or more transfusions to combat this toxic manifestation.

Haematuria has not been reported in the course of therapy with sulphanilamide but is quite frequent when sulphapyridine or sulphathiazole is being used. Haematuria may be either microscopic or gross and may be a precursor of severe renal insufficiency. We have generally considered it best to stop the drug if haematuria makes its appearance, but in several instances we have observed patients in whom haematuria developed and in whom the continuance of therapy did not result in any grave kidney lesion.

Anuria with concurrent azotemia has not been reported in the course of sulphanilamide therapy but has been noted in the course of treatment with sulphapyridine or sulphathiazole. The anuria may be due to a true toxic injury of the tubules of the kidney, probably similar to that seen in mercury bichloride poisoning, or it may be due to the deposition of acetylsulphapyridine or acetylsulphathiazole crystals in the kidney tubules, and on occasion to the blocking of the renal pelvis and ureters by calculi composed of acetylsulphapyridine or acetylsulphathiazole.

If anuria makes its appearance, fluids should be forced by mouth and by the parenteral route. If vomiting is present, sodium chloride should be given by mouth or in the form of physiologic solution of sodium chloride by the parenteral route, because it is important to prevent hypochloremia from developing. If the anuria persists for more than twenty-four hours, the ureters should be carefully catheterized, and if obstruction is found an attempt should be made to wash out the ureters and renal pelvis gently with warm physiologic solution of sodium chloride in order to remove the renal calculi. If obstruction is not present, fluids should be forced, and in our experience all such patients have eventually recovered from this toxic manifestation of the drug.

Hyperleukocytosis has been seen in this series of cases only when acute haemolytic anaemia has been present. We have noticed total white blood cell counts ranging as high as 90,000 cells in the presence of acute haemolytic anaemia. These very high white blood cell counts probably represent an abnormal response of the bone marrow to a hurried call made on it by the rapidly developing anaemia. In this connection one should always remember that many nucleated red blood cells are being thrown into the circulation and that an allowance should be made for this fact in calculating the total white blood cell count.

Purpura haemorrhagica has not been seen in any of our cases but it has been reported as occurring in the course of therapy with sulphanilamide and sulphapyridine. If this toxic manifestation is noted, the drug should be stopped and fluids forced.

An injection of the scleras and conjunctivas, which may be so severe as to resemble 'pink eye', has been noted quite frequently in the course of sulphathiazole therapy. It generally occurs between the fifth and the ninth day of treatment with this drug, and its appearance is often heralded by burning and smarting of the eyes.

Other ocular and auditory disturbances, such as visual and auditory hallucinations and changes in visual and auditory acuity, have been noted in the course of sulphanilamide therapy, but they are rare.

Painful joints have been reported in the course of sulphanilamide therapy, and we have noted that several patients who have received sulphathiazole have had exquisitely tender, swollen joints. This toxic manifestation may be puzzling when the patient is suffering from gonorrhoea because of its resemblance to acute gonorrhoeal arthritis.

Stomatitis has been encountered rarely in the course of sulphanilamide therapy, while unexplained bleeding from the gastro-intestinal tract has been seen by us on one or two occasions in cases in which sulphanilamide or sulphapyridine was being administered. One patient who was receiving sulphapyridine had such severe bleeding as to bring about death. Occasionally cases are encountered in which the administration of sulphanilamide produces severe attacks of diarrhoea.

#### COMMENT

It is obvious from this description of the toxic manifestations of sulphanilamide and its derivatives that certain deductions can be made. We believe that, whenever possible, it is wise to utilize every available means of laboratory control in following patients who are receiving sulphanilamide or one of its derivatives. White blood cell counts, haemoglobin and urine examinations should always be done when circumstances permit this type of control. However, we are convinced that, with the exception of acute leucopenia, all the toxic manifestations of sulphanilamide or its derivatives which may occur in the first two weeks of therapy can be recognized by careful clinical observation, and we feel that no physician should hesitate to administer these drugs in therapeutically adequate amounts, provided he can see his patient at least once a day.

At the time the physician visits the patient who is receiving one of these drugs he should inquire as to his symptoms, especially in respect to headache, body aching or malaise, because these symptoms are often

the precursors of many of the toxic reactions of sulphanilamide or its derivatives. In addition to an inquiry about symptoms, the scleras should be examined for the presence of jaundice, the mucous membranes for pallor and the skin for evidences of rash. The temperature should always be taken in order to detect whether drug fever is present, and if the patient says that he has been having chills and at the time that it is taken the temperature is normal, arrangements should be made to have the temperature taken frequently during the next twenty-four hours in order to determine whether or not fever is present.

No special precautions have to be observed in respect to the urine of patients who are receiving sulphanilamide, but it is highly important that the urine of patients who are receiving sulphapyridine or sulphathiazole be measured daily. This does not mean that the attendants or family of the patient have to record the urine volume in cubic centimetres or ounces, but any standard measure, whether it is only cups, will suffice. As a matter of fact, in the case of infants it would probably be satisfactory to record the number of voidings daily. In this way it is possible to detect an oliguria which may herald an approaching anuria. The daily examination of the urine under these circumstances should consist of a careful examination of a fresh specimen for gross blood, and at the same time instructions should be given to the patient's attendants to stop the drug and administer fluids in large quantities if the urine looks bloody.

Finally, one should always remember that if a patient has once had drug fever, rash, hepatitis, leukopænia, acute hæmolytic anæmia, injection of the scleras and conjunctivas, diarrhœa or purpura hæmorrhagica in the course of therapy with sulphanilamide or its derivatives he is very likely to have a second, earlier and more severe toxic reaction if the drug is administered a second time. Therefore it is highly important to determine whether or not a patient has previously had a toxic reaction in the course of therapy with one or the other of these drugs. If he gives a history of a toxic reaction in the group which we have just enumerated, it is best to give a small test dose of the drug (0.3 gm.) and observe the patient carefully over a period of twelve hours before cautiously beginning the course of therapy. Patients who have had a toxic reaction caused by one of these drugs may have a similar reaction when another member of the sulphonamide group is prescribed.

### Photograph of a Sneeze

(From *Public Health Reports*, Vol. LV, 19th July, 1940, p. 1315)

SANITARIANS have long known that certain diseases are spread by the discharges from the mouth and nose, and that droplet infection plays a rôle in the dissemination of pathogenic micro-organisms. They have also known that such micro-organisms may be discharged into the air in greater numbers and to greater distances by the uncovered cough and sneeze than in ordinary breathing. But since such droplets are not visible under ordinary conditions, the risks of infection by this means have not been fully appreciated by the public, and the precautionary warnings of health officers to 'cover your cough and your sneeze' are not generally heeded.

If any one has failed to appraise fully the potential danger of spreading infection to others by an uncovered sneeze, he has only to study the accompanying photograph, taken by Prof. M. W. Jennison, of the Department of Biology and Public Health, Massachusetts Institute of Technology, which shows the expulsion of droplets in a violent, unstified act of sneezing.

According to Dr. C. E. Turner, who furnished the photograph, the picture was taken by the technique of ultra high-speed photography, which substitutes an instantaneous flash of light for the opening and closing of the camera shutter. This stroboscopic light illuminates the object to be photographed with an intense

flash of short duration, the light being placed in such a position in this picture as to illuminate the droplets with a dark-field effect, so that they stand out sharply even in daylight and give photographic images larger than actual droplet size. The time of exposure was about 1/30,000 of a second.

In such a sneeze as that illustrated here, the droplets are numbered in the thousands, varying with the intensity of the expiratory effort. The number of bacteria dispersed in a sneeze may also be very large. It is stated that most of the droplets are under 2 mm. in diameter and that many are less than 0.1 mm.

The 'muzzle velocity' of some droplets is said to be as great as 150 feet a second, and large droplets may be expelled to a distance of 12 feet, although the majority do not travel more than 2 or 3 feet. The involuntary closing of the mouth near the end of a sneeze tends to form a restricted orifice, resulting in the production of more and smaller droplets, which probably come largely from the saliva in the front of the mouth. Also it is apparent from the photograph that the number of droplets issuing from the nose in an unstified sneeze is insignificant as compared with the number expelled from the mouth. As stated by Jennison and Edgerton, these observations are probably important in relation to infectivity, because of the differences in the microbic flora of the two regions.

Some droplets fall to the floor or ground, while others evaporate, leaving their bacteria suspended in the air,



The expulsion of droplets in an unstified sneeze.

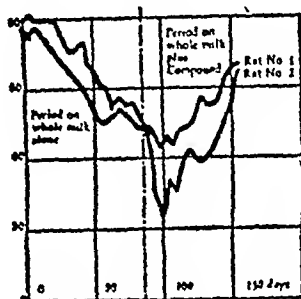
through which they may be disseminated by air currents.

The bacteriologic and epidemiologic aspects of infection of the air were discussed in a recent article by Wells, Wells, and Mudd, who conducted experiments on the concentration of micro-organisms in the air. They state that 'the numbers of streptococci characteristic of the nasopharynx indicate a hazard of respiratory infection and have a sanitary significance comparable with the presence of *Escherichia coli* in drinking water'. They estimate that several thousand nasopharyngeal streptococci per sneeze are contributed to the atmosphere and that 'the sneeze thus almost seems to be a provision of nature for the survival of nasopharyngeal parasites. Even where the manifestations of a disease do not provide for the wide auto-dissemination of the infection through the air it has been observed that an outbreak of colds will be followed by the rapid spread of contagion. Sneezing induced by pollens might conceivably facilitate the spread of nasopharyngeal infection . . .'

Although much is yet to be learned experimentally regarding the physical and other characteristics of expiratory droplets which are factors in determining more accurately the rôle of droplet transmission in those communicable diseases that are spread by nose and mouth discharges, there can be no question that covering the mouth in coughing and sneezing is an important preventive measure with respect to such diseases.

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**THACKER SPINK . . . CALCUTTA**



## Fluid for the Surgical Patient

(From the *Lancet*, Vol. II, 17th August, 1940, p. 199)

THE fluid loss of the body in health varies widely, with occupation and environment among other things, but Starling puts the normal loss for the average adult at  $4\frac{1}{2}$  pints a day, of which about  $2\frac{1}{2}$  pints is lost in the urine,  $1\frac{1}{5}$  pint in the faeces, and the remainder by insensible perspiration from the skin or as water vapour from the lungs. The surgical patient often has a big fluid deficit to make up, and during and after operation perspiration is much increased; 6 to  $6\frac{1}{2}$  pints a day is therefore a reasonable allowance for the immediate post-operative period. In addition to water the patient needs salt and glucose, but Avery Jones and Naunton Morgan point out that salt may easily be overdone. They suggest 5 g. daily as a sufficient allowance of salt, and if the 6 to  $6\frac{1}{2}$  pints of fluid are given in the form of normal saline the patient will get over 30 g. of salt, which he may have difficulty in excreting. The retention of salt may then lead to the accumulation of water in the tissues which may produce subcutaneous oedema or water-logging of the lungs and delay the healing of wounds. Normal saline is therefore unsuitable for prolonged administration, but it is useful in replacing electrolytes lost by vomiting or sweating. For rectal infusion Jones and Morgan recommend normal saline diluted with four parts of tap water (0.18 per cent NaCl), though tap water alone is often sufficient and is well tolerated. For continuous intravenous infusion the solution is made up of one part of normal saline and four parts of 5 per cent glucose in distilled water.

This solution contains 0.18 per cent NaCl and 4 per cent glucose, and is isotonic. Hypertonic saline has a strictly limited application in surgery apart from its use as a diuretic and for reducing intracranial pressure, but it is of value in cases of paralytic ileus where there is stagnation of fluid in the dilated intestinal loops. More complicated solutions such as Ringer's and Hartman's have had a certain vogue, but they are unnecessary in most surgical cases.

If the patient can and will drink and there is no other contra-indication the fluid should be given by the mouth. This obvious principle is sometimes forgotten. In comatose or unco-operative patients the fluid can be given by a tube passed into the stomach

through the nose or mouth. After the mouth the rectum is probably the next best route, and up to 10 pints can usually be given daily in this way by a continuous drip delivering not more than 30 to 40 drops a minute, using a small rubber catheter (no. 9) but occasionally a feeble ill patient cannot tolerate the catheter or retain the fluid in his rectum. Nowadays it is the fashion to pour fluid straight into a vein, but this has some serious disadvantages. It is fatally easy to give too much fluid or to give it too quickly, for by this route the blood stream has no choice but to take what is given it. Moreover, as Walthers has remarked, the saline is mixed directly with the blood and thus reduces still further the concentration of plasma proteins which will already be low after an operation, whereas fluid given by the mouth or rectum passes through the liver first, and will be able to pick up protein *en route* before entering the pulmonary circulation. Inserting a needle or cannula into a vein may be difficult for the inexperienced, especially in a collapsed patient, the subsequent infusion needs careful watching, and the needle often needs readjustment or even reinsertion. Hypodermolysis is easy but not much fluid can be given by this route; there is also great danger of infection, and glucose solutions may cause aseptic necrosis. Intraperitoneal infusion is seldom used except in babies, for it is risky and has few advantages.

Lately, Billimoria and Dunlop have described a simple method of administering fluids intramuscularly. The only special instrument required is a long strong needle fitted with a sliding shield. Little skill or time is needed for inserting the needle and setting up the apparatus. If two needles are used—one in each thigh—more than 8 pints of fluid can be given in a day and infusion by this route has been maintained continuously for eight days. If the fluid is given too rapidly it is held up as local oedema, thus safeguarding the pulmonary and systemic circulations against dangerous flooding or dilution. Infection is rarely encountered if strict aseptic precautions are observed. Glucose in 5 per cent solutions may safely be given in this way, but care must be taken that none of the solution collects in the subcutaneous tissues. This method is not new and its soundness is well established; it deserves to be more widely adopted.

## Reviews

**RECENT ADVANCES IN ENDOCRINOLOGY.**—By A. T. Cameron, M.A., D.Sc. (Edin.), F.I.C., F.R.S.C. Fourth Edition. 1940. J. and A. Churchill, Limited, London. Pp. viii plus 432, with 67 figures, including three plates. Price, 18s.

ENDOCRINOLOGY is one of the most virile of the medical sciences, and after a period of four years there are enough 'recent advances' to fill a whole volume. The author has however interpreted the term in the more liberal manner and has interwoven his account of the advances of these four years with that of the advances of the last decade or so. Most of the important sections have been completely rewritten and certain obsolete matter deleted, but the net result is an increase of about 20 per cent in the printed matter. There has been a 25-per-cent increase in the matter on each page without loss to readability; this has allowed an actual reduction in the number of pages.

One of the most important advances in the last four years has been the synthesis of a number of hormones. The physician is liable to accept these chemical triumphs too lightly, but he cannot ignore their practical importance. One example is desoxycorticosterone acetate;

though it has not entirely displaced gland-extracted cortin, which also probably acts by virtue of its impurities, it can at least be used as a substitute for this expensive gland product in a number of occasions, and it may mean that the man of moderate means with Addison's disease will be kept alive as a useful member of society for a considerable time. A reference in this volume is made to a patient who was maintained in almost normal health for at least two years with 25 c.cm. of cortin daily, but, to compensate for the labour involved in preparing this amount of gland extract, the individual would have to be a very valuable member of society. Another advantage of the synthetic preparation is that tablets can be inserted subcutaneously for maintenance dosage.

Equally important advances have been made in the realm of sex hormones and here again synthetic preparations are well established.

The impression that one gains from reading this important review on the present status of endocrinology is that, if the science is not prostituted by adventurer manufacturers and advertisers and the too-easily-victimised polytherapy-practising members of the profession, it has a very bright future.

**DERMATOLOGIC ALLERGY: AN INTRODUCTION IN THE FORM OF A SERIES OF LECTURES.—**

By M. B. Sulzberger, M.D. 1940. Charles C. Thomas, Springfield, Illinois. Pp. xxii plus 540, with 13 coloured plates and 39 illustrations. Price, 47s. Obtainable from Messrs. Ballière, Tindall and Cox, London

THIS book is arranged as a series of fourteen lectures. The first is devoted to definitions and classification of skin allergy, and the second is on the protective nature of the skin and its importance as a possible originator of allergic changes. Lecture three is on the basic phenomena in allergy and lecture four describes how to investigate a suspected case of skin allergy.

These four lectures make an excellent introduction to the study of this difficult subject, and having acquired that knowledge the student is next taken through the principal types of allergic skin reaction in the next nine lectures, and lecture fourteen is an interesting and speculative consideration of the future of allergy in medicine.

At the end of the book there are several appendices one of which is particularly useful as it gives a long alphabetically-arranged list of substances used in patch tests with the strengths of the solutions and the solvents it is best to use for each of them, and another appendix of practical value is one of 30 pages in which the general management of urticarial and eczematous conditions is discussed, apart from their allergic aspect.

The author modestly describes his book in the opening sentence of the preface by saying it is not a book of reference nor an encyclopædic treatise on allergy. On this account it is all the more useful to the average practitioner who is concerned primarily with treating and curing his cases, because he can obtain from its pages more than he will usually need in the treatment of allergic skin diseases, without having to flounder through a welter of irrelevant and often contradictory statements such as a complete reference book on allergy must contain.

It is a book we can heartily recommend to all those who want a working knowledge of allergic dermatitis and how to treat it, and at the same time they will acquire a sufficient insight into the scientific aspect of the subject to show what a fascinating field it offers to those with inquiring minds.

P. A. M.

**ROSE AND CARLESS MANUAL OF SURGERY: FOR STUDENTS AND PRACTITIONERS.—**

By C. P. G. Wakeley, D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S., and J. B. Hunter, M.C., M.Chir. (Cantab.), F.R.C.S. (Eng.). Sixteenth Edition. Volumes I and II. 1940. Ballière, Tindall and Cox, London. Pp. xi plus 840 in volume I and pp. from 841 to 1708 and 48 index pages in volume II. Price, 30s. for two volumes

'ROSE AND CARLESS' is too well known to students and teachers to require a lengthy introduction. Except for one gap due to the last war, revisions of this textbook have been made at three-yearly intervals, and it is now in its sixteenth edition. But comparison of this with the two previous editions reveals that very important improvements have been made.

In the first volume, the first eight chapters show considerable alteration and now provide a concise introduction to surgical pathology which it would be hard to equal. For the rest, new descriptions of neurosurgery and much-needed revision in the section on fractures deserve special mention.

There are many new illustrations, and some of the old ones have been redrawn; they are perhaps of greatest value in the chapters on abdominal surgery, and include a coloured plate depicting gastroscopic appearances.

In the chapter on hernia the following passage is to be found: 'The most satisfactory operation of all for inguinal hernia, and that associated with the least number of recurrences, is some modification of Gallie's operation.' This is at variance with the opinion of many teachers, and also with a remark made by the

senior editor in his Hunterian lecture on 31st January, 1940, which reads, 'During the last few years fascial grafts for the repair of an inguinal hernia have come into vogue, and it has been claimed that the results are better than by other methods. I cannot agree that this view . . .' (*vide The Lancet*, 4th May, 1940, p. 822).

As before, the second volume contains chapters on special subjects by various contributors, and the section on tropical surgery has again been written by Sir Frank Connor.

Two new chapters attract special attention. The first is an excellent one on anaesthetics by Dr. Vernon Hall. If anaesthetists in this country would put into practice some of his teachings, the lot of both surgeon and patient would be immeasurably improved. The other chapter, the last in the book, is devoted to war surgery. In it the editors have laid down the general principles of this branch for the guidance of medical officers on active service.

Although larger and more profusely illustrated than before, the price of this book remains the same, so that one has no hesitation in predicting its continued popularity.

W. McN. N.

**SHOCK: BLOOD STUDIES AS A GUIDE TO THERAPY.—**

By John Scudder, M.D., Med., Sc.D., F.A.C.S. 1940. J. B. Lippincott Company, Philadelphia and London. Pp. xvii plus 315, with 55 illustrations, 5 plates—3 of which are in colour. Price, 30s.

THIS book is a record of experimental work on shock. It is also incidentally an historical bibliography of earlier work, and it will always justify its shelf-room on account of its bibliography of 533 references, and its historical record of the developments in our conception and treatment of shock, and in our knowledge of the functions of the adrenal gland and of the physiological effects of potassium. The author's own work could however have been reported more concisely and therefore more usefully in a reasonably-sized article in some journal devoted to experimental medicine.

One of the main contentions of the writer is that careful blood examination in each case is essential as a preliminary to proper treatment. One of the effects of shock is hæmoconcentration, which can be shown by an increase in specific gravity, but this may be associated with an actual loss in the proportion of red cells to the circulating blood, which will be indicated by a cell volume estimation. He might go further and suggest that a total red cell count should always be done, for after hæmorrhage there is an increase in size of the individual red cell, so that an increase in cell volume might cover a loss in numbers of red cells and an actual decrease in cell-plasma interface.

Another point made is the increase in plasma potassium in shock and also in stored blood, so that obviously the latter is unsuitable for use in shocked patients, and plasma separated at an early date would be much better.

The volume is a beautiful example of the best American book production and the writer's style is lucid, though he lapses now and then into the jargon of the careless medical writer, *e.g.*, 'at the time of her operative death'. What would A. P. H. say?

**DISEASES AFFECTING THE VULVA.—**

By Elizabeth Hunt, B.A., M.D., Ch.B. (Liverpool). 1940. Henry Kimpton, London. Pp. xiii plus 215, with 36 illustrations and 18 plates in colour. Price, 21s.

A book such as Dr. Hunt's 'Diseases Affecting the Vulva' is very welcome indeed, and Dr. Hunt may rest assured that it will 'prove of assistance in the treatment of the many women who suffer so seriously and so long', the hope she expresses in her preface.

After an introduction, in which allergy is very clearly explained, the anatomy and development of the vulva are described. There is an excellent chapter on the histology of the vulval tissues and then the author goes on to the description of all those diseases which

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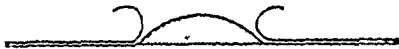
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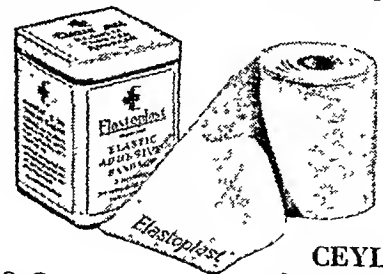
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affect the vulva. Each condition is taken completely under the headings 'Ætiology', 'Clinical Manifestations', 'Diagnosis' and 'Treatment' and where necessary 'Complications', 'Histopathology' and so on are added. The descriptions are clear and concise, and really portray pictures. The author, though not dogmatic, is definite in her opinions on controversial subjects. Treatment is expounded particularly well and includes useful prescriptions for nearly all conditions. Considering the reputation skin diseases have for chronicity a little more space might be devoted to prognosis which is rarely mentioned, except by implication. For example, in discussing the treatment of kraurosis, the author advises the use of vegetable rather than mineral oils 'as these patients may require to use the preparations daily for a prolonged period'. Whether or not a cure is to be hoped for is not mentioned.

The pictures, so clearly described in the text, are supplemented by 28 really beautiful coloured plates and there are, in addition, 36 figures mostly of microscopic sections.

This book, so far as I know the only one of its kind, should be read and kept for reference by all who attempt the treatment of women. This is especially true in India where dermatologists are few and far between and where, unfortunately, skin conditions are often very inadequately treated. Pruritus, the subjective symptom, is more often than not labelled pruritis, a disease, and treated with douches, tampons, and alkaline hip-bath. This may not only fail to relieve the itching but may, as Dr. Hunt emphasizes, do actual harm.

G. B. W. F.

**MEDICAL DISEASES OF WAR.**—By Sir Arthur Hurst, M.A., D.M. (Oxon.), F.R.C.P., Lieut.-Colonel, late R.A.M.C. With the Co-operation of H. W. Barber, M.A., M.B. (Cantab.), F.R.C.P., F. A. Knott, M.D. (Lond.), M.R.C.P., and T. A. Ross, M.D. (Edin.), F.R.C.P. 1940. Edward Arnold and Company, London. Pp. viii plus 327. Illustrated. Price, 16s.

THIS book deals with the medical diseases that are the results of or are encountered during wars, and it is based on the author's varied experience of these diseases during the last great war and the post-war period.

More than half of the book deals with the various aspects of war neurosis. These chapters, which contain numerous illustrative case notes, are the results of original studies that Sir Arthur Hurst carried out among the soldiers of the last great war, and they form a brilliant exposition of the subject. Besides war neurosis, some acute infectious diseases, skin diseases, war nephritis, gas poisoning—the other diseases that are likely to be encountered in an European war—have been adequately discussed. Some of the diseases that are likely to occur in a tropical campaign have not been described in this book. This is unfortunate, for the present war is no longer limited to Europe, but has spread to tropical countries.

The book is written by one of the most eminent men in the medical profession in England and the various chapters written by him bear the stamp of a master of the subject. The author has invited collaboration of well-known specialists in writing some of the special sections. This has further enhanced the usefulness of this single volume dealing with the various diseases of war.

The book will undoubtedly be of help to medical officers called upon to treat soldiers and civilians during the present war.

P. C. S. G.

**A MANUAL OF EMBRYOLOGY: THE DEVELOPMENT OF THE HUMAN BODY.**—By J. Ernest Frazer, D.Sc. (Lond.), F.R.C.S. (Eng.). Second Edition. 1940. Baillière, Tindall and Cox, London. Pp. x plus 523, with 282 Illustrations. Price, 30s.

NINE years ago when Professor Frazer produced the first edition of *Manual of Embryology* he departed

from the traditional method of taking each and every organ separately and describing its development. He introduced the new method of giving as far as possible regional descriptions. This has not only made the book enjoyable to read, but it gives a clear picture of the growth of the body as a whole and not as he says 'a patchy series of discrete descriptions of the formation of organs'.

Another departure was the omission of references and the failure to point it out always when the author's descriptions deviated from those then generally accepted. Since then Professor Frazer's views on development have become universally known and the student will never be far wrong if he accepts them *in toto*.

The drastic cutting down of detail, the author states in his preface, is not pleasant. This is indeed true, more detail would be welcome in every section.

One disadvantage of the regional method—which is really an asset—is that the student swatting for his anatomy examination is unable to turn up the textbook and learn off an embryological note for each organ. This was a very popular method of 'learning embryology'. Actually it is not too much to hope that any student trying to use Frazer's *Embryology* in this manner will become interested in the subject and really learn something; certainly the text is sufficiently interesting to hold the attention of the serious student if once he dips in. Some space devoted to the various abnormalities of development would add to this interest and would be appreciated in the next edition.

The 1940 edition is on the same plan as the first edition though there are minor changes in its arrangement and some additions including seven new diagrams and new accounts of the umbilical cord, foetal circulation, and the sinus venosus.

Few misprints have been carried over into the new edition, for example, on page 169 in the penultimate sentence 'hind-brain' has been written instead of 'mid-brain', and, in figure 7, U.C. has been used to identify two different things, the umbilical cord and the uterine cavity.

The paper and printing in the new edition are distinctly superior.

G. B. W. F.

**FORENSIC CHEMISTRY.**—By Henry T. F. Rhodes, Dip. Inst.C. (Lyon). 1940. Chapman and Hall, Limited, London. Pp. viii plus 214. Price, 12s. 6d.

THIS little book by a worker in France covers remarkably well the ground common to the police and the chemist. It is much more than the toxicology which is usually associated with forensic medicine. References are plentiful and will provide, when necessary, details of procedures.

With a view to increasing the utility of the next edition of this useful book the following suggestions are offered: (i) removal of certain obscurities (p. 13, third para.; p. 95 last para.; p. 175 first para.) and an unnecessary restriction (p. 176, not keeping sulphuric acid in glass bottles); (ii) differentiating between blood *groups* and blood *types*; (iii) clarification of description by rearranging headings and sub-headings and indicating them by the usual system of lettering or numbering (a heading in CAPITAL letters should not be a part of a narrative under a heading in small letters, an instance on p. 129, and items whose relationship is one of genus and species should not be headed alike when following one another, an instance on p. 183); and (iv) inclusion of sweat analysis undertaken for turf clubs (samples from horses suspected to have been drugged have been sent to France for many years from all over the world).

The paper, the printing and the binding are good. Only one printer's error arrests attention (p. 121 last para. 'd oments'). The price perhaps could be lowered in normal times.

The book should be available to all investigators of crime.

S. D. S. G.



1938—a decline of 121 deaths. Of the total number of infantile deaths, 1,461 (46.91 per cent) were amongst the Burmese, 839 (26.94 per cent) amongst the Hindus, 333 (10.69 per cent) amongst the Mohammedans and 247 (7.93 per cent) amongst the Chinese. The important causes of infantile mortality were as usual convulsions, bronchitis and pneumonia, premature birth, malnutrition, dysentery and diarrhoea and enteritis.

Four thousand seven hundred and sixty-five infants were under the care of the Maternity and Child Welfare Scheme of this department and out of these, 634 died giving a mortality rate of 133.05 per 1,000 against 177.51 in the year 1938. The table below gives the infantile mortality rate amongst infants under the care of the Maternity and Child Welfare Scheme in the city during the last 4 years.

1936	..	145.96	1938	..	177.51
1937	..	139.90	1939	..	133.05

The tuberculosis dispensary maintained its popularity, the number of new patients and the total attendance during the year being 4,927 and 38,039 respectively compared with 3,955 and 34,206 during the previous year.

The number of patients treated at the various other dispensaries maintained by the Corporation was 183,691 compared with 172,087. The total attendances at these dispensaries during the year was 435,910 against 403,582 during the previous year.

There is not much to report with regard to any improvement made in the milk supply of the city. Two thousand four hundred and eighty samples of milk, of which 2,394 were taken by the milk inspectors, were examined. Eight hundred and nineteen conformed to the standard.

The water supply, as usual, was chlorinated and kept at a high standard of bacteriological purity. During the year, treatment of water by chloramine was tried. The results were encouraging but in view of the difficulties of obtaining regular supplies of chemicals as a result of the war, further progress could not be made although chloramine treatment is still being continued.

The staff employed for combating the mosquito nuisance in the city continued to do useful work. The public has now become conscious of the mosquito problem and if sustained efforts are made, the day is not distant when the mosquito problem will become practically insignificant.

#### ANNUAL REPORT ON THE WORKING OF THE ASSAM MENTAL HOSPITAL, TEZPUR, FOR THE YEAR 1939

THE superintendent has endeavoured, with considerable success, to introduce the modern 'hospital' outlook into the institution, as opposed to the out-of-date 'Lunatic Asylum' atmosphere. The keeper staff have been taught the ideal that inmates of the institution are sick patients and that the proper attitude towards them is that of a nurse in a children's hospital. According to modern ideas of psychological medicine as much freedom as is compatible with safety is given to the patient and mechanical restraint has been done away with. This has, of course, put considerable strain on the staff, but it seems well justified.

Dr. H. C. Barua, the Superintendent, remarks—

'This institution is a mixture of an asylum, a jail and a mental hospital. The majority of the patients are chronic cases requiring life-long asylum treatment. Those cases, however, in whom there is a prospect of cure react adversely during the recovery process, when they are in association with chronic cases. This is also observed as in the case of criminal mental patients who may, after recovery, have to stay in association with chronic cases sometimes for a considerable period before their discharge. These patients fully realize their position and some relapse. For such cases a separate convalescent home is wanted and it is suggested that the two new blocks proposed as a future extension should be built outside the compound and devoted to this purpose'.

The points raised by the superintendent are important and deserve the consideration of Government.

*Paying patients.*—There were only six patients among the inmates, at the time of submitting the report, who were stated to be capable of paying modest rate of maintenance. This seems an incredibly small proportion.

*Sanitation and hygiene.*—The defects here are outstanding and have been reported repeatedly. It is almost unbelievable that an institution of this kind, the only one in Assam, should have to carry on its work with a totally inadequate water-supply and with an antiquated arrangement for sterilizing clothing and bedding.

The municipal water-supply, in spite of the high tax charged, is, and seems likely to remain, totally insufficient and a separate plant for the hospital with a good tube-well is essential. Insufficient water brings the inevitable sequel of dirt and disease, and nowhere is it more important to guard against these than in a community composed mainly of mental patients.

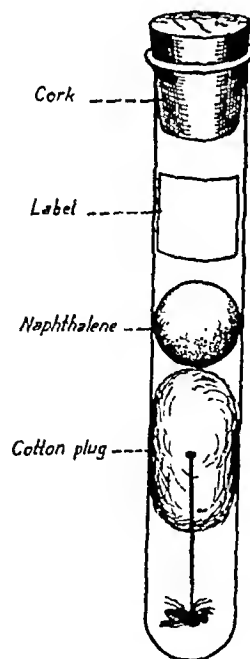
The 'blanket boiler' can only be described as a relic of the past. It should be abolished and replaced by a modern type of steam sterilizer. Efficient sterilizing and perhaps even more important here—effective—delousing is otherwise impossible.

## Correspondence

### ENTOMOLOGICAL SPECIMENS

To the Editor, THE INDIAN MEDICAL GAZETTE

SIR,—For a number of years, I have made use of the following plan to demonstrate entomological specimens to students:—



A stout test-tube of suitable width is selected. The specimen to be mounted is picked up on a long entomological needle, and absorbent cotton-wool is wrapped round the shaft of the needle till the cotton forms a closely-fitting bung; the whole is then introduced into the test-tube, the insect being foremost. The cotton plug is carefully pushed in till the specimen is very near the dome-shaped bottom of the test-tube. A naphthalene ball is put in, and the proper label



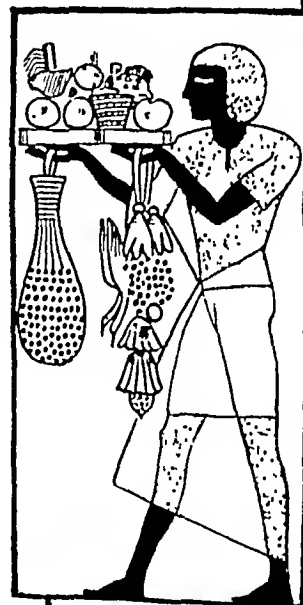
# During the Age of Growth

**A**T no time, throughout the span of life, is the proper and orderly balance of calcium, phosphorus and iron, vitamins and other highly important food elements more readily disturbed than during the period of active growth and development.

The food supply of every child should, therefore, contain an adequate proportion of these important substances, if normal progress is to be maintained. The construction of an entirely correct dietary, to suit the varying requirements of each individual is, however, beyond the possibility of realization in ordinary practice.

Many physicians ensure that the ordinary dietary of the young patient is safe and adequate by advocating the daily addition of 'Ovaltine'. This is a complete, well-balanced food, rich in natural vitamins and in readily assimilable calcium, phosphorus and iron.

'Ovaltine' is composed of ripe barley malt, pure creamy cow's milk together with valuable natural phosphatides and vitamins. Its sugar content is chiefly in the form of maltose, a very readily available source of energy. No cane sugar or chocolate is added to give bulk or to cheapen the cost. 'Ovaltine' is delightful to the taste and readily assimilable even by digestions impaired by disease.



## 'OVALTINE'

TONIC FOOD BEVERAGE

M287

*A liberal supply for clinical trial sent free on request :*

*Indian Distributors :*

Grahams Trading Co. (India), Ltd., 6, Lyons Range, Calcutta, also at Bombay, Madras and Karachi.

*Servants of high official bearing offerings to the Tomb.*

# ST. BARTHOLOMEW'S HOSPITAL OPERATION TABLE

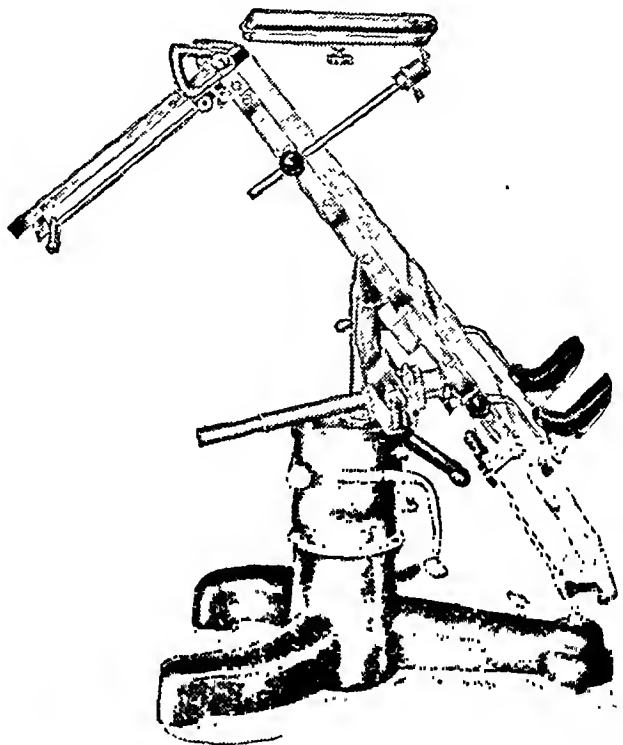
with the  
**Latest Improvements**

including

Easy to operate Release Lever for lowering the table; Trendelenburg position increased to 55° tilt; Foot operated rubber-covered Floor Brake.

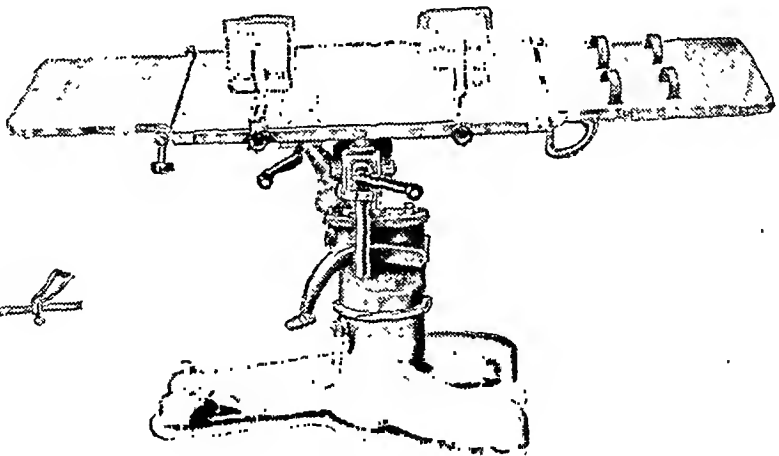
The St. Bartholomew's Hospital Operation Table is now manufactured in five different models and thus supplies a range of modern operation tables embodying the latest ideas of well-known surgeons for carrying out surgical operations.

All models can be supplied with either tripod or platform base.



**Model A**

In Trendelenburg position, 55° tilt, showing shoulder rests and instrument tray in position.



**Model AC**

in lateral position, with back elevator and lateral supports.

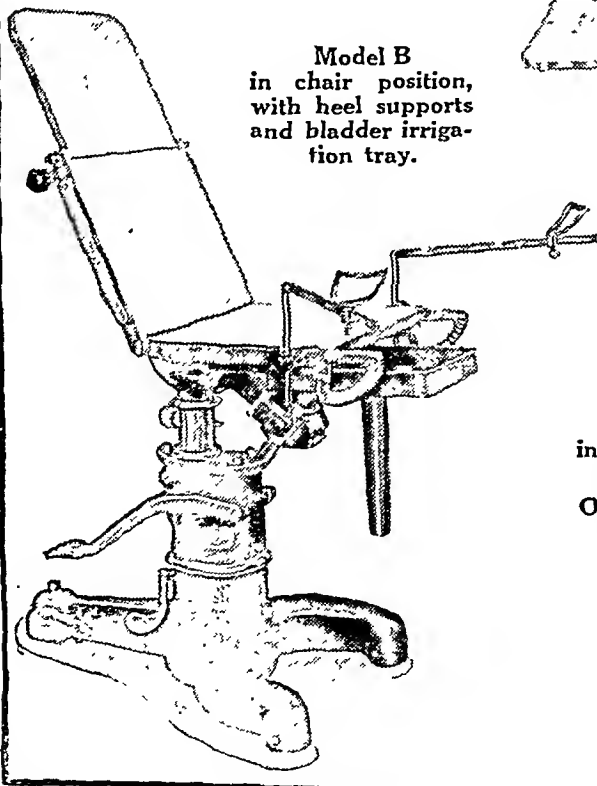
Over 1075 of these tables are in use at home and abroad.

*A descriptive booklet, fully illustrated, will be sent on request.*

**ALLEN & HANBURY LTD.**

(Incorporated in England)

**CLIVE BUILDINGS, CALCUTTA**  
and at 37 Lombard Street, London, E.C.3



**Model B**  
in chair position,  
with heel supports  
and bladder irriga-  
tion tray.

giving name, details, etc., is then introduced. A cork or rubber stopper completes the mounting.

Thus preserved, the specimens last for years, and each can be examined in detail with a hand-lens.

I have found that this method saves a lot of time and temper, as heads and legs do not drop off so frequently, and the mounting is able to withstand the onslaught of a series of classes.

Yours, etc.,

P. A. DALAL, L.M. & S. (Bom.),  
D.T.M. & H. (Camb.),  
(Late Professor of Bacteriology,  
Grant Medical College, Bombay).

242, PRINCESS STREET,  
BOMBAY,  
24th October, 1910.

## Service Notes

### APPOINTMENTS AND TRANSFERS

COLONEL R. H. CANDY, C.I.E., K.H.S., is appointed to be Surgeon-General with the Government of Bombay, with effect from the 31st October, 1910.

Lieutenant-Colonel R. S. Aspinall, C.I.E., an Agency Surgeon, is appointed as Residency Surgeon, Mysore, with effect from the afternoon of the 15th October, 1910.

Lieutenant-Colonel M. Das, M.C., made over the executive charge of the Alipore Central Jail to Mr. C. Heath on the afternoon of the 4th October, 1910.

Lieutenant-Colonel F. H. Whyte is appointed to the post of Civil Surgeon, New Delhi, with effect from the forenoon of the 15th October, 1910.

Major E. A. R. Ardeshtir made over charge of the office of Superintendent of Rajshahi Central Jail to Dr. Monsural Rahman on the afternoon of 4th October, 1910.

On return from leave Major D. W. B. Read, an officer of the Medical Research Department, is transferred to foreign service under the Indian Research Fund Association, with effect from the 8th July, 1910 (forenoon).

Major G. Milne, an officiating Agency Surgeon, is appointed as Medical Officer in charge of the Crown Representative's Police Force Hospital, Neemuch, with effect from the forenoon of the 16th October, 1910.

The undermentioned officers retire with gratuity and are granted emergency commissions from the dates specified against each:—

#### Short Service Commission

Captain R. Kasliwal. Dated 23rd September, 1910.

#### Permanent Commission

Captain A. S. Rao. Dated 10th October, 1910.

#### To be Captains (on probation)

Tahil Dayaram Chablani. Dated 30th September, 1910, with seniority from 30th September, 1936.

Ram Lal Soota. Dated 10th October, 1910, with seniority, 10th October, 1936.

Motilal Shankhla. Dated 11th October, 1910, with seniority, 11th October, 1936.

#### To be Lieutenants (on probation)

Thomas Jenner Powell. Dated 3rd August, 1910.

#### Emergency Commissions

##### To be Lieutenants

3rd August, 1910

William Hope Stanislaus St. John-Brooks.  
John Maurice French.  
Malcolm Shaw.

William Raynard Smith.  
Gerald Charles Tresidder.  
Ronald Houston Vasey.

15th August, 1910

Chandra Nath Chatterji.  
Kshirode Bihari Roy.  
Mohamed Abdul Razak.  
Parmeshwar Lal Khurana.  
Edaseril Kesava Pillai Kesava Pillai.  
Siti Kantha Misra.  
Amalekhandra Chattopadhyay.  
Prasanta Kumar Das.  
Gurbachan Singh Lamba.  
Pabitra Kumar Paul.  
Trikovil Variyathu Ramankutty Wariyar.  
Ronald Sushil Chandra Banerji.  
Gurtej Singh Dhaliwal.  
Chenckuppam Thangavelu Subrahmanyam.  
Ranjit Kumar Chatterjee.  
Ram Sarikhan Prasad Sinha.  
Srinivasanallur Matrubhutam Venkatakrishnan.  
Sachindra Nath Bose.  
Subbarama Piclumani.  
Anwar-ul-Islam.  
Uma Prasad Das Gupta.  
Jacob Jacob.  
Biswanath Barat.  
Hem Chandra Sen Gupta.  
Jyotsnananda Sen.  
Pooran Singh.  
Aduma Dharar.  
Mohammad Suleman.  
Nand Lal Sharma.  
Padminjarail Zachariah Abraham.  
Bansi Lal Aggarwal.  
Vidya Sagar Sharma.  
Mir Mohammad Sharif.  
Satya Prakash.  
Chandar Bhan.  
Krishna Chandra Majumdar.  
Gaya Kumar.  
Harjinder Singh Malik.  
Kodaganallur Srinivasa Rama Sramu.  
Irshad Ali Sahibzada.  
Janki Nath Dhar.  
Mohammad Alam.  
Goraysahib Abdul Alcem.  
Birendra Kishore Go-swami.  
Nirod Ranjan Gupta.  
Victor Frederick Siqueira  
Jatish Chandra Sen.

16th August, 1910

Nallakandy Vydier Sridharan.  
Sudhindra Nath Bose.  
Pulin Behari Bose.  
Sudhir Kumar Das.  
Suhas Chandra Chatterjee.

17th August, 1910

Indu Bhusan De.

1st September, 1910

Baroda Kanta Bhadury.  
Yoginder Singh Bawa.  
Dines Chandra Roy.  
Kunikuttan Ramakrishnan.  
Polichetti Umamaheswara Rao.  
Krishna Pillai Balakrishna Menon.  
Puttiah Rama Raju.  
Kitianda Calappa Ganapathy.  
Thottungal Krishnan Rithuparnan.  
Doulatabad Narayanrao Madhava Rao.  
Kannanur Puthan Madhathil Bhavadasan Unni Nayar.  
Krishnaswami Siva Rama Krishnan.  
Kattoju Paidilingam.  
Vadilal Purshotamdas Patel.  
Srinivasan Sivarajan.  
Gopal Das.  
Joti Ranjan Sen.  
Shib Chandra Sarkhel.

Champadil Chandrasekhara Menon.  
 Kunnariath Gopala Menon.  
 Ramalinga Iyer Ananthanarayanan.  
 Ayyub Ahmad Khan.  
 Nazir Ahmad.  
 Pudukottah Sivaramakrishna Viswanathan.  
 Behari Lal Kamra.  
 Gadahad Vasudeva Rao.  
 Pagadala Damodram.  
 Bashir Ahmad.  
 Kaipuzha Narayanan Nair Sankaran Nair.  
 Sangram Singh.  
 Subbier Ganapathi Sundaram.  
 Mohammad Hanif Ahmed.  
 Abdul Jabbar.  
 Har Kishan Lal.  
 Mohammad Qamaruddin.  
 Sukhdes Lal Rikhye.  
 Mahmud Husain Qazi.  
 Edward Norish Chander Benjamin.  
 Subal Chandra Chatterjee.  
 Des Raj Batura.  
 Tejindar Singh Khurana.  
 Bishan Kishore.  
 Bishan Chand Bhalla.  
 Susil Chandra Mazumdar.  
 Radha Krishnan Arora.

#### LEAVE

Major-General H. C. Buckley, K.H.P., Surgeon-General with the Government of Bombay, is granted leave on average pay for 1 month and 24 days followed by leave on half-average pay for 2 months and 6 days, with effect from 31st October, 1940.

Lieutenant-Colonel J. B. Hance, C.I.E., O.B.E., an Agency Surgeon, is granted leave for 2 months, with effect from the afternoon of the 15th October, 1940.

#### PROMOTIONS

The undermentioned General Officers are granted the local rank of Lieutenant-General:—

3rd October, 1940

Major-General W. H. Hamilton, C.B., C.I.E., C.B.E., D.S.O., K.H.P., D. M. S. in India.

Major-General G. G. Jolly, C.I.E., K.H.P., Director-General, Indian Medical Service.

*Major to be Lieutenant-Colonel*

F. H. Whyte. Dated 17th October, 1940.

*Captains to be Majors*

F. M. Khan. Dated 3rd April, 1939.

H. Min Sein. Dated 26th July, 1939.

A. W. West. Dated 3rd August, 1939.

S. P. Bhatia. Dated 12th October, 1939.

J. O'Neill. Dated 23rd April, 1940.

M. K. Bryce. Dated 3rd August, 1940.

J. L. O'Neill. Dated 3rd August, 1940.

W. J. Stewart. Dated 3rd August, 1940.

M. Ata-ullah. Dated 20th October, 1940.

#### RETIREMENT

Lieutenant-Colonel G. C. Maitra. Dated 10th November, 1940.

## Notes

### GLAXO LABORATORIES PRODUCTS

We have just received a very neat catalogue of the products of this laboratory.

The first dozen pages or so are conveniently devoted to indices. The first is an index of their products in alphabetical order: they cover a wide range and include over sixty items. The next is a pharmaceutical index from 'threatened abortion' in which 'viteolin', an extract of wheat germ oil, which is rich in vitamin E,

to 'wounds' for which they recommend 'flavogel', acriflavine jelly. This index refers to well over a hundred diseases in which Glaxo products are useful. There is then a separate list of vitamin products, from A to P, and finally detailed lists of Pharmaceutical Products, 'Glaxo' Injections, Dissolved Vaccines 'Glaxo' and Glaxo Food Products, with full details of indications and dosage.

This is a very handy list for any doctor to keep on his table for quick reference. The agents, H. J. Foster & Co., Ltd., have offices in Calcutta (P. O. Box 2257), Bombay (P. O. Box 202), Madras (P. O. Box 108) and Lahore (P. O. Box 244).

### UREA SULPHAZIDE:—'T'

(U. S. T.)

UNION DRUG Co., Ltd., take pleasure to announce the introduction of their latest chemotherapeutic, UREA SULPHAZIDE:—'T' (U. S. T.), designed for the oral treatment of gonococcal infections. Clinical trials with the preparation have shown that it is equally effective in the treatment of all stages of gonorrhoea and its complications.

Samples of the product and fuller details on dosage and method of administration are supplied to the medical profession on request to the manufacturers at 285, Bowbazar Street, Calcutta.

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# HEWLETT'S ORIGINAL PREPARATIONS

## HEWLETT'S MIXTURE

(Mist. Pepsinae Co. c. Bismutho.)

COMPOSITION :—Pepsine, Bismuth, Sol. Opii Purif., Tr. Nuc. Vom., Acid Hydrocyanic Dil., etc.

Over 60 years' reputation as a useful remedy in Dyspepsia especially when Pyrosis is a conspicuous symptom and in Diseases of the Stomach.

DOSE :—One to two drachms, diluted.

Price in England. 4-oz. bottles, 10d. oz. 10, 22, 40, and 90-oz. bottles, 12/6 per lb.

## LIQ. ERGOTAE PURIF. (HEWLETT'S)

Physiologically standardised. This preparation is superior to the ordinary liquid extracts, tinctures and other preparations of Ergot. It has been successfully employed in tedious Labours, Post-Partum Hæmorrhage, Hæmoptysis, Dysmenorrhœa, etc., and also in the treatment of Whooping Cough.

Price in England. 5, 10, 22, 40, and 90-oz. bottles, 25/- per lb.

## MIST. ANTI-ASTHMATIC CONC. (HEWLETT'S) 1 to 7

COMPOSITION :—Potassii Iodid., Sodii Brom., Ext. Euphorb. Pilulif., Nitro-Glycerine, 1/200 gr.; Tinct. Lobeliae, etc., in each fluid ounce.

This mixture is prepared from the recipe of the eminent therapist, Dr. Hare, for the relief of Asthma and its concomitants, dyspnœa, sibilant bronchi, loud wheezing or shrill whistlings.

DOSE :—One fluid ounce of the diluted mixture.

Price in England. 4-oz. bottles, 4d. oz. 10, 22, 40, and 90-oz. bottles, 4/6 per lb.

## "HEPATAGEN" TRADE MARK

(Mist. Hepatica Conc. Hewlett's)

An excellent compound of Cascara, Rhubarb, Jalap, Podophyllin, etc. with 1/20 gr. Cocaine in each drachm.

(Not under the Dangerous Drugs Act.)

An elegant and palatable general Aperient and Cholagogue, especially recommended in cases of so-called "Biliousness", Hepatitis and Chronic Gastritis.

DOSE :—10 to 60 minims, diluted.

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## LIQ. SANTAL FLAV. c. BUCHU et CUBEBA (HEWLETT'S)

The original preparation. Containing three remedies of proved utility and employed with extraordinary success in certain cases.

DOSE :—One to two drachms in peppermint water.

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## MIST. DAMIANAE CO. (HEWLETT'S)

Recommended for Neurasthenia, also in the Dyspepsia of commencing Phthisis. It soothes the stomach and enables the patient to take more food whilst acting as a powerful stimulant in relieving exhaustion.

Price in England. 4-oz. bottles, 10d. oz. 10, 22, 40, and 90-oz. bottles, 12/6 per lb.

**C. J. HEWLETT & SON, LTD., 35 to 42, Charlotte Road,  
LONDON, E. C. 2.  
Established over a Century**

# HORLICKS

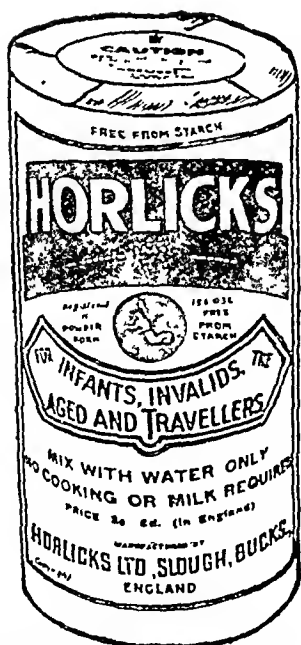
## IN PNEUMONIA

**H**ORLICKS is fresh, full-cream cows' milk combined with the nutritive extracts of wheat and malted barley.

During pneumonia and other acute fevers of short duration the amount of nourishment taken by the patient is not of primary importance, though liquid food at frequent intervals is of value.

Horlicks is an ideal form of nourishment during these illnesses. It is easily and simply prepared—requiring the addition of water only. Hence, no more than is sufficient for a meal need be made at any one time, and the patient is thus assured of receiving freshly prepared food in an appetising form.

Horlicks is easily digested and readily assimilated; it contains adequate protein and possesses marked protein-sparing qualities. It thus prevents tissue waste, and is a valuable builder during convalescence.



# HORLICKS

*Available Everywhere*



# TRIMAX

(STEARNS)

*Hydrated Magnesium Trisilicate*

ANTACID • ANTIPEPTIC • ANTITOXIC

A smooth, white, fine powder in which no evidence of grit can be detected by the teeth or tongue. It is tasteless and insoluble, possessing adsorbent and antacid properties of particular value in the treatment of Gastric Hyperacidity and Chronic Peptic Ulceration of the Stomach, Duodenum, and Jejunum.

Available in bottles containing 1½ ounces by weight. Owing to the levity of the powder this is equivalent to 8 ounces by volume.

*Distributors for Bengal :*

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Bonfield Lane : CALCUTTA

*Agents :*

**MARTIN & HARRIS LTD.**

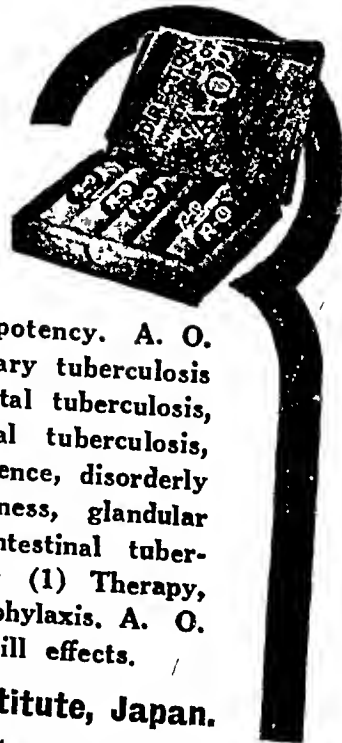
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*Discovered by:*  
**Prof. R. ARIMA**

A. O. is made from Tubercle Bacilli of the human type. It is sterile, consists of the native protoplasm of the bacilli, is absorbed, is completely innocuous, is derived from strongly immunizing strains of bacilli and has a uniform potency. A. O. is indicated in cases of latent tuberculosis, pulmonary tuberculosis (apical catarrh), surgical tuberculosis and urogenital tuberculosis, ophthalmological tuberculosis, dermal tuberculosis, pleurisy and peritonitis, in convalescence, disorderly menstruation due to innate weakness, glandular affections, laryngeal and intestinal tuberculosis. A. O. is used for (1) Therapy, (2) Diagnosis, and (3) Prophylaxis. A. O. is innocuous and has no ill effects.



*Made by :* The Arima Institute, Japan.

*Complete literature can be had from the Sole Agents :*

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*Yes*, mathematics is an exact science—but one does not always equal one.

For relief of chronic asthma, one injection of Adrenalin in Oil is frequently equivalent to five of aqueous Adrenalin. Relief with the oil suspension often persists ten hours; the effect of the aqueous solution lasts not more than two hours.

Basic Adrenalin is much less soluble than Adrenalin Chloride, and difference in time of action (between two such pre-

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Except in emergencies, where the rapid action of aqueous Adrenalin is desirable, symptomatic therapy of asthma, urticaria, and serum sickness is advantageously carried out with Adrenalin in Oil.

Adrenalin in Oil, a 1:500 suspension of basic Adrenalin in peanut oil, contains 2 milligrams of hormone in each cubic centimeter.

*Supplied in 1-cc. ampoules, boxes of 6.*

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